In the United States Court of Federal Claims

OFFICE OF SPECIAL MASTERS
No. 16-0265V
Filed: August 23, 2021
PUBLISHED

ALICIA LEANN BOHN, on behalf of her deceased minor child, G.B.,

Petitioner,

v.

SECRETARY OF HEALTH AND HUMAN SERVICES,

Respondent.

Special Master Horner

Sudden Infant Death Syndrome (SIDS); Dismissal; Insufficient Proof

Patricia Ann Finn, Patricia Finn, P.C., Nanuet, NY, for petitioner.
Laurie Wiesner, U.S. Department of Justice, Washington, DC, for respondent.

DECISION[1]

On February 25, 2016, petitioner, Alicia Bohn, filed a petition under the National Childhood Vaccine Injury Act, 42 U.S.C. § 300aa-10-34 (2012)[2] on behalf of her minor child, G.B., alleging that several routine childhood vaccinations, including Haemophilus influenzae type B (Hib), pneumococcal conjugate (Prevnar), rotavirus (Rotateq 3), and Pediarix,[3] administered on March 12, 2014, "caused-in-fact" his death on March 13, 2014. (ECF No. 1.) On June 29, 2020, petitioner filed a motion for a ruling on the written record. (ECF No. 51.) For the reasons set forth below I find that petitioner is not entitled to compensation.

[1] Because this decision contains a reasoned explanation for the special master's action in this case, it will be posted on the United States Court of Federal Claims' website in accordance with the E-Government Act of 2002. *See* 44 U.S.C. § 3501 note (2012) (Federal Management and Promotion of Electronic Government Services). **This means the decision will be available to anyone with access to the Internet.** In accordance with Vaccine Rule 18(b), petitioner has 14 days to identify and move to redact medical or other information the disclosure of which would constitute an unwarranted invasion of privacy. If the special master, upon review, agrees that the identified material fits within this definition, it will be redacted from public access.

[2] Within this decision, all citations to § 300aa will be the relevant sections of the Vaccine Act at 42 U.S.C. § 300aa-10-34.

[3] Pediarix is a combined vaccine including diphtheria, tetanus, acellular pertussis, hepatis B, and inactivated poliovirus. *See* https://www.fda.gov/vaccines-blood-biologics/vaccines/pediarix (last visited August 19, 2021).

I. Applicable Statutory Scheme

Under the National Vaccine Injury Compensation Program, compensation awards are made to individuals who have suffered injuries after receiving vaccines. In general, to gain an award, a petitioner must make a number of factual demonstrations, including showing that an individual received a vaccination covered by the statute; received it in the United States; suffered a serious, long-standing injury; and has received no previous award or settlement on account of the injury. Finally – and the key question in most cases under the Program – the petitioner must also establish a *causal link* between the vaccination and the injury. In some cases, the petitioner may simply demonstrate the occurrence of what has been called a "Table Injury." That is, it may be shown that the vaccine recipient suffered an injury of the type enumerated in the "Vaccine Injury Table," corresponding to the vaccination in question, within an applicable time period following the vaccination also specified in the Table. If so, the Table Injury is presumed to have been caused by the vaccination, and the petitioner is automatically entitled to compensation, unless it is affirmatively shown that the injury was caused by some factor other than the vaccination. § 300aa-13(a)(1)(A); § 300 aa-11(c)(1)(C)(i); § 300aa-14(a); § 300aa-13(a)(1)(B).

In many cases, however, the vaccine recipient may have suffered an injury *not* of the type covered in the Vaccine Injury Table. In such instances, an alternative means exists to demonstrate entitlement to a Program award. That is, the petitioner may gain an award by showing that the recipient's injury was "caused-in-fact" by the vaccination in question. § 300aa-13(a)(1)(B); § 300aa-11(c)(1)(C)(ii). In such a situation, of course, the presumptions available under the Vaccine Injury Table are inoperative. The burden is on the petitioner to introduce evidence demonstrating that the vaccination actually caused the injury in question. *Althen v. Sec'y of Health & Human Servs.*, 418 F.3d 1274, 1278 (Fed. Cir. 2005); *Hines v. Sec' of Health & Human Servs.*, 940 F.2d 1518, 1525 (Fed. Cir. 1991).

The showing of "causation-in-fact" must satisfy the "preponderance of the evidence" standard, the same standard ordinarily used in tort litigation. § 300aa-13(a)(1)(A); *see also Althen*, 418 F.3d at 1279; *Hines*, 940 F.2d at 1525. Under that standard, the petitioner must show that it is "more probable than not" that the vaccination was the cause of the injury. *Althen*, 418 F.3d at 1279. The petitioner need not show that the vaccination was the sole cause of the injury or condition, but must demonstrate that the vaccination was at least a "substantial factor" in causing the condition, and was a "but for" cause. *Shyface v. Sec'y of Health & Human Servs.*, 165 F.3d 1344, 1352 (Fed. Cir. 1999). Thus, the petitioner must supply "proof of a logical sequence of cause and effect showing that the vaccination was the reason for the injury." *Id*. at 1353. The logical sequence must be supported by "reputable medical or scientific explanation, *i.e*., evidence in the form of scientific studies or expert medical testimony." *Althen*, 418 F.3d at 1278; *Grant v. Sec'y of Health & Human Servs.*, 956 F.2d 1144, 1148 (Fed. Cir. 1992). A petitioner may not receive a Vaccine Program award based solely on his or her assertions; rather, the petition must be supported by either medical records or by the opinion of a competent physician. §300aa-13(a)(1).

In what has become the predominant framing of this burden of proof, the *Althen* court described the "causation-in-fact" standard, as follows:

> Concisely stated, Althen's burden is to show by preponderant evidence that the vaccination brought about her injury by providing: (1) a medical theory causally connecting the vaccination and the injury; (2) a logical sequence of cause and effect showing that the vaccination was the reason for the injury; and (3) a showing of proximate temporal relationship between vaccination and injury. If Althen satisfies this burden, she is "entitled to recover unless the [government] shows, also by a preponderance of the evidence, that the injury was in fact caused by factors unrelated to the vaccine."

Althen, 418 F.3d at 1278 (citations omitted). The *Althen* court noted that a petitioner need not necessarily supply evidence from medical literature supporting petitioner's causation contention, so long as the petitioner supplies the medical opinion of an expert. *Id*. at 1279-80. That expert's opinion must be "sound and reliable." *Boatmon v. Sec'y of Health & Human Servs*., 941 F.3d 1351, 1359-60 (Fed. Cir. 2019). The *Althen* court also indicated, however, that a Program fact finder may rely upon "circumstantial evidence," which the court found to be consistent with the "system created by Congress, in which close calls regarding causation are resolved in favor of injured claimants." *Althen,* 418 F.3d at 1280.

In her petition, petitioner did not allege a specific fatal injury to G.B. that was caused in fact by his March 12, 2014 vaccinations.[4] (ECF No. 1.) However, in her motion for a ruling on the record, petitioner contends that the release of cytokines caused "endothelial damage resulting in hemorrhaging and congestion in multiple organs," which caused G.B.'s death. (ECF No. 51, p. 1, 20-21.) Because these injuries are not listed on the Vaccine Injury Table, petitioner must satisfy the above-described *Althen* test for establishing causation-in-fact.

II. Procedural History

Petitioner filed her petition on February 25, 2016. (ECF No. 1.) The case was initially assigned to Special Master Laura Millman, who has since retired. (ECF No. 4.) Petitioner subsequently filed medical records on March 10 and April 11, 2016. (ECF Nos. 5, 8.) At the initial status conference, petitioner advised that she intended to provide an expert report from a pediatric pathologist. (ECF No. 9.)

On September 26, 2016, petitioner filed an expert report from Dr. Laurel Waters. (ECF No. 12; Ex. 12.) During a second status conference, petitioner was advised that

[4] The autopsy report reflects an official cause of G.B.'s death as "probable asphyxia due to co-sleeping." (Ex. 4 at 1.)

Dr. Waters's report did not fulfill petitioner's burden of preponderant evidence.[5] (ECF No. 13.) Respondent's counsel reported that her client had retained a pediatric immunologist to provide an opinion. (*Id.*) Respondent was ordered to file this expert report, along with a Rule 4(c) report. (*Id.*)

Thereafter, respondent filed his Rule 4(c) report, arguing that the evidence presented did not meet petitioner's burden and recommending against compensation. (ECF No. 17.) Concurrently, respondent also filed expert reports from Dr. Christine McCusker (immunology) and Dr. Sara Vargas (pathology). (ECF No. 17; Exs. A, C.) Petitioner was then permitted to file a supplemental report from Dr. Waters and another expert report from Dr. Douglas Miller. (ECF No. 22; Exs. 22, 23.) Respondent subsequently filed a supplemental report from Dr. McCusker. (ECF No. 26; Ex. NN.) Petitioner then filed a supplemental report from Dr. Miller. (ECF No. 28; Ex. 24.) Finally, on November 28, 2017, respondent filed a supplemental report from Dr. Vargas. (ECF No. 29; Ex. OO.)

During a telephonic status conference on January 10, 2018, petitioner was ordered to submit a demand to respondent. (ECF No. 30.) However, in a status report dated June 11, 2018, respondent advised that, "given his strong views on the causation issue in this matter, he does not wish to negotiate a settlement." (ECF No. 37.) On that same date, Special Master Millman issued an order indicating that "when this case is transferred to another special master upon [her] retirement, the new special master will schedule a hearing date." (ECF No. 38.)

After this case was reassigned to my docket on June 6, 2019 (ECF No. 42), I ordered the parties to confer and file a joint status report confirming that the case remained ripe for a hearing given the recent Federal Circuit ruling in *Boatman v. Secretary of Health & Human Services*, 941 F.3d 1351 (Fed. Cir. 2019). (ECF No. 44.) The parties thereafter filed a status report indicating that "they are amenable to either a ruling on the existing record, or proceeding to a hearing in this matter, at [my] discretion." (ECF No. 45.) After reviewing the case, I determined that a ruling on the written record was appropriate and ordered the parties to propose a briefing schedule.[6] (ECF No. 46.)

Petitioner filed a motion for a ruling on the record on June 29, 2020. (ECF No. 51.) Respondent filed his response to petitioner's motion on November 9, 2020 and petitioner filed her reply to respondent's response to petitioner's motion on January 12, 2021. (ECF Nos. 56, 59.) This case is now ripe for a ruling on the record.

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[5] Dr. Waters's report will be discussed in detail below. The statement discussed during the status conference was her conclusion that the "three different arms of the immune response which are active in the first 24 hours [after vaccination] cause cytokine production, which *could* become excessive and cause a lethal cytokine storm." (Ex. 12 at 10 (emphasis added).)

[6] That is, I have concluded that the record is sufficiently developed and the parties have had a full and fair opportunity to present their respective cases. *Kreizenbeck v. Sec'y of Health & Human Servs.*, 945 F.3d 1362, 1366 (Fed. Cir. 2020); *see also* Vaccine Rule 8(d); Vaccine Rule 3(b)(2).

III. Factual History

a. Medical Records and Petitioner's Affidavit

G.B. was born via c-section at 39 weeks on January 14, 2014. (Ex. 1, p. 5-6.) There were no complications. (*Id*.) G.B. received his first hepatitis B vaccination on the date of his birth. (*Id*. at 8.) Petitioner had a mostly unremarkable pregnancy but had risks due to smoking, having undergone prior cesarean delivery, and having less than one year between pregnancies. (*See generally*, Ex. 7.)

On January 16, 2014, G.B. had his first newborn visit with Dr. Edward Legako. (Ex. 2, p. 1.) At both this appointment and at another appointment on January 20, 2014, G.B. was noted to be feeding well and gaining weight appropriately. (*Id*. at 3.) On January 29, 2014, G.B. returned to Dr. Legako for diarrhea over the preceding week, but physical examination was unremarkable. (*Id*. at 5.) Petitioner was reassured that G.B.'s stool was normal for a breastfeeding infant and was advised that G.B. continued to gain weight appropriately. (*Id*.) On March 12, 2014, G.B. had his two-month well child visit with Dr. Legako, and he received routine childhood vaccinations (DTaP, hepatitis B, IPV, HIB, pneumococcal 13, and rotavirus). (*Id*. at 7, 9.) During this visit, Dr. Legako assessed G.B. with normal growth, nutrition, development, and behavior. (*Id*. at 7-8.)

In her affidavit, petitioner indicates that after G.B. received his vaccinations, he cried "hysterically" and then "passed out" while they were still at the pediatrician's office. (Ex. 3 at 1.) After awakening later in the day, he continued to cry and "seemed absolutely miserable" before falling asleep for approximately four hours. (*Id*. at 2.) G.B. awoke two times during the night, during which he was crying and unwilling to nurse more than "two to three swallows." (*Id*.) After his second awakening, sometime between 4:30 and 5:00 a.m., petitioner placed G.B. next to her in her bed. (*Id*.) Petitioner awoke at 8:45 a.m. and found G.B. "lifeless." (*Id*.)

On the morning of March 13, 2014, the Sterling Volunteer Fire Department was dispatched to petitioner's residence pursuant to a call that G.B. was "unconscious [and] not breathing." (Ex. 10 at 1.) When the fire department arrived, G.B.'s father (a member of the fire department) was already performing CPR. (*Id*. at 2.) CPR was continued for approximately "20 to 25 minutes." (*Id*.) A Sterling Police Department Attended/Unattended Death Report prepared by Mike Barker[7] lists G.B.'s time of death as 9:57 a.m. on March 13, 2014.[8] (Ex. 9 at 4.). G.B.'s body was taken directly to the Oklahoma City Office of the Chief Medical Examiner. (*Id*. at 5.)

On April 9, 2014, Petitioner completed and submitted a form to the Vaccine Adverse Event Reporting System (VAERS). (Ex. 8 at 1.) She described the adverse event as "death, within 24 hours." (*Id*.)

[7] Mr. Barker is an officer with the Sterling Police Department. (Ex. 9 at 4.)

[8] The "Report of Investigation by Medical Examiner" lists the time of death as 9:47 a.m. (Ex. 4 at 5.)

b. Autopsy Reports

Dr. Ruth Kohlmeier of the Office of the Chief Medical Examiner of Oklahoma City performed an autopsy of G.B. at approximately 1:00 p.m. on March 14, 2014. (Ex. 4 at 1.) The manner of death was determined to be accidental and the cause of death was identified as "probable asphyxia due to co-sleeping." (*Id.*) Post-mortem toxicology was negative. (*Id*. at 1, 5.) Dr. Kohlmeier's examination revealed no traumatic findings but did reveal fixed livor mortis, both anteriorly and posteriorly. (Ex. 4 at 1-2; Ex. 20.) There was purple lividity of the left side of the face and blanching of the right side of the face. (Ex. 4 at 2.) During internal examination, G.B.'s brain, lungs, liver, and spleen were noted to be "heavy for age." (*Id*. at 2-3.) There was also a small amount of petechial hemorrhages on the lungs; while microscopic examination showed marked atelectasis and congestion. (*Id*. at 3-4.)

Petitioner subsequently requested a second opinion from another pathologist. Petitioner (?) sent sixteen autopsy slides and Dr. Kohlmeier's report to Dr. Steven Rostad. (Ex. 5.) Dr. Rostad's findings included vascular congestion of the adrenal gland, lungs, liver, pancreas, brain, and leptomeninges; acute hemorrhages of the kidney and adrenal gland; acute intra-alveolar hemorrhage; atelectasis; and granular ependymitis. (*Id*. at 1) Dr. Rostad further commented that "[t]ypical microscopic findings of vaccination-related adverse reaction are not seen, however [this] does not exclude such a cause in my opinion" and that "[o]verall, the findings are not specific but could be explained by asphyxia." (*Id*.)

IV. Expert Reports

a. Petitioner's Experts

i. Douglas Miller, M.D., Ph.D.

Petitioner presented an opinion by neuropathologist, Douglas C. Miller, M.D., Ph.D., to support her claim. (Ex. 22.) Dr. Miller received his medical degree from University of Miami School of Medicine in 1974 and his doctorate degree in physiology and biophysics from University of Miami in 1978. (Ex. 21.) Dr. Miller is board certified in anatomic pathology and neuropathology by the American Board of Pathology. (Ex. 21, p. 3.) Dr. Miller practices as a neuropathologist at University of Missouri Healthcare and as a contract physician/consultant for the Department of Pathology at Harry S. Truman Veterans Hospital. (Ex. 22, p. 2.) Additionally, Dr. Miller currently holds a teaching position at University of Missouri School of Medicine. (Ex. 21 at 3.) In this position, he acts as the neuropathologist for the Office of the Chief Medical Examiner for two counties in Missouri and provides forensic pathology services to many counties in Missouri that have non-physician or non-pathologist coroners. (Ex 22 at 2.) Dr. Miller has also authored numerous publications relating to neurology and neuropathology. (Ex. 21 at 6.)

In his role as a forensic pathologist for medical examiner offices, Dr. Miller is frequently consulted in cases with sudden unexpected death of infants and young children, so he has "considerable (and lengthy) experience in the pathological analysis of Sudden Infant Death Syndrome (SIDS) and Sudden Unexpected Death in Childhood (SUDC)." (Ex. 22 at 2.)

In opining that vaccines contributed to G.B.'s death, Dr. Miller acknowledges that the risk factors[9] that are typical in SIDS cases would statistically make SIDS the most likely scenario in this case, but the lack of histopathological abnormalities of G.B.'s medulla and the presence of the marked congestion and hemorrhage seen in multiple organs argue against this conclusion.[10] (Ex. 22 at 5-6.) He therefore concludes that "this case does not fit the most common SIDS scenarios, vaccinations or no vaccinations (or at least as far as the autopsy evidence permits, it does not fit)." (*Id*. at 6.) Dr. Miller also disagrees that G.B.'s death was due to asphyxiation. (*Id*.)

Instead, Dr. Miller contends that, after reviewing the autopsy slides, the findings in G.B.'s organs "suggest a diagnosis . . . of an acute visceral microvascular bleeding disorder, which is an abnormality that is likely mediated by cytokines, with some similarities to primary or secondary 'capillary leak syndromes.'" (*Id*. at 5). Dr. Miller notes that Petitioner's affidavit suggests that G.B. began to behave abnormally as soon as he was vaccinated. (*Id*. at 6.) Specifically, Dr. Miller opines that "the only reasonable hypothesis for [G.B.'s] altered behavior, including excessive sleepiness, fussiness/crying, and refusal to feed, is a process mediated by the innate immune system, one resulting from cytokines, which are generally regarded as the mediators of so-called 'sick behavior.'" (*Id*. at 7.) He further notes that the autopsy showed a "widespread petechial hemorrhagic process," which he contends is most likely the result of cytokine actions "even if the precise mechanism remains to be elucidated." (*Id*. at 7-8.)

Despite acknowledging the lack of explanation for the mechanism of action, Dr. Miller postulates that the severe congestion with hemorrhages in many of G.B.'s organs "implicates a diffuse systemic cytokine-mediated problem of small vessel (capillary) integrity." (Ex. 22 at 8.) He suggests that a condition known as "systemic capillary leak syndrome" (SCLS)[11] can provide insight into how it is more likely than not that G.B.'s

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[9] These include prematurity, male sex, maternal smoking during pregnancy, exposure to tobacco smoke in the dwelling, prone sleeping, hyperthermia, co-sleeping, and mild upper respiratory infections. (Ex. 22 at 5-6.)

[10] Dr. Miller characterizes G.B.'s lungs as "severely congested." (Ex. 22 at 4.) However, as will be discussed in more detail below, Dr. Vargas, one of Respondent's experts, contends that G.B.'s lungs appeared consistent with what one would expect to find in an infant who received CPR and whose cause of death was determined to be asphyxia. (Ex. OO at 4.)

[11] SCLS was first described as an idiopathic condition in which adults had single or multiple episodes had single or multiple episodes of otherwise unexplained swelling of the peripheral tissues (including muscle tissue). (Robin, Eugene et al., *Capillary Leak Syndrome with Pulmonary Edema*, Arch. Int. Med., 1972; 130:66-71 (Ex. 34).) SCLS will be discussed in more detail below.

vaccinations triggered a cytokine response that resulted in his death. (*Id*.) Dr. Miller indicates that the pathophysiology of SCLS has been thought to involve cytokines of the same species documented to be secreted in response to vaccinations. (*Id*.) Therefore, Dr. Miller asserts that it is plausible that G.B.'s vaccinations triggered a cytokine response, similar to that experienced by patients with SCLS, "which for reasons unknown set off a cascade of events" resulting in endothelial damage and the hemorrhages and congestion in multiple organs as found at autopsy, and causing G.B.'s death. (*Id*.)

After submitting his initial expert report, Special Master Millman requested a supplemental report discussing whether the basis for Dr. Miller's opinion on causation would change absent petitioner's affidavit regarding G.B.'s behavior after he received the vaccinations. (ECF No. 25). In a letter dated October 30, 2017, Dr. Miller states, "I would say that the history given by [petitioner] as to [G.B.'s] abnormal behavior is of some importance, because it suggests that there was an ongoing abnormal cytokine response beyond that usually accepted for routine vaccinations." (Ex. 24.) However, he further notes that his interpretation of the autopsy findings and conclusions as to their most likely cause, as well as the cause of death, would not change if the symptoms and signs reported by petitioner were not present. (*Id*.)

ii. Dr. Laurel Waters, M.D.

Petitioner also presented an opinion by Dr. Laurel Waters, a pediatric pathologist and assistant clinical professor at the University of California at Davis School of Medicine, Department of Pathology and Laboratory Medicine. (Ex. 11 at 1.) She received her medical degree from the University of California at Davis and is board certified in pediatric pathology, anatomic and clinical pathology, and nuclear medicine. (*Id*.) She also has extensive clinical laboratory experience. (*Id*. at 2-3.)

In her report, Dr. Waters questions the medical examiner's assessment of G.B.'s cause of death as probable asphyxia due to co-sleeping. (Ex. 12 at 6.) She contends that asphyxia is difficult to diagnose from a clinical perspective, and G.B. "was not shown by any autopsy findings to have definitely died due to asphyxia." (*Id*. at 6, 10.) Dr. Waters further asserts that co-sleeping is not a cause of death, but instead should be characterized as a risk factor and only in the context of when an adult is impaired by alcohol or drugs. (*Id*.)

In contrast to the medical examiner's assessment, Dr. Waters opines that the multiple vaccinations[12] administered to G.B. "massively stimulat[ed] his immune

[12] Dr. Waters initially incorrectly listed one of the vaccines received by G.B. and the expected immune response. (Ex. 12 at 8.) Specifically, Dr. Waters reported that G.B. received Pneumovax 23, not Prevnar. (*Id*.) Prevnar is a conjugated (rather than pure polysaccharide) vaccination. (Ex A at 5.) The immune response to Prevnar is similar to that seen with the HiB vaccine, another conjugated vaccination. (*Id*. at 5.) Dr. Waters corrected this error in her supplemental expert report. (Ex. 23 at 2.)

system," activating three different arms[13] of the immune response and causing cytokine production. (Ex. 12 at 7-10.) She states that if an excess of cytokines occurs in any one or any combination of the three arms, it could be enough to produce a lethal cytokine storm. (*Id*. at 10.) In addition, Dr. Waters postulates that because G.B. had previously been exposed to hepatitis B (when he was vaccinated shortly after birth), he "likely suffer[ed] from an anamnestic response to it, causing a more serious reaction, setting him up for a cytokine storm" when combined with the cytokines released after the other vaccinations. (*Id*. at 8, 10.)

Citing the example of dengue fever, Dr. Waters indicates that cytokine storms can cause both increased inflammation and an increased capillary permeability syndrome, similar to the SCLS discussed by Dr. Miller. (Ex. 12 at 9.) Dr. Waters further suggests that susceptibility to cytokine storm is variable, such that it is impossible to predict who will respond poorly and who will overrespond. (*Id*. at 10.) While Dr. Waters acknowledges in her supplemental report that it was possible that G.B. did not suffer an actual cytokine storm, she maintains that "the increase in cytokines precipitated by the immunizations caused [his] death." (Ex. 23 at 4.)

b. Respondent's Experts

i. Christine McCusker, MSc, M.D., FRCP

Respondent's first expert, Dr. McCusker, holds a Master of Science degree in molecular biology and an M.D., both received from McMaster University in Ontario, Canada. (Ex. B at 2.) She is board certified in both pediatrics and allergy and clinical immunology. (*Id*. at 3.) She currently serves as an associate professor of pediatric allergy and immunology at McGill University and as Division Director of Pediatric Allergy, Immunology, and Dermatology at the Montreal Children's Hospital. (*Id*. at 4.)

In her initial report, Dr. McCusker specifically addresses Dr. Waters's conclusion that G.B. suffered from a fatal vaccine-mediated cytokine storm. (Ex. A at 4.) To begin, Dr. McCusker acknowledges that vaccination is predicted to activate immune responses in part through cytokine upregulation. (*Id*. at 6.) However, the magnitude of cytokine responses induced by vaccination are much lower than in natural infection because the innate system is comparatively poorly activated. (*Id*. at 5.)

Dr. McCusker reports that local cytokine effects include pain and redness at the site of inoculation and systemic cytokine effects include fever and malaise. (Ex. A at 4.) In fact, she explains that while vaccination is predicted to activate immune responses in part through cytokine upregulation, there is no evidence to suggest that these "post-vaccination" cytokines exist at levels sufficient to influence the development of a cytokine storm as hypothesized by Dr. Waters. (*Id*. at 6). Dr. McCusker further notes that no literature supports Dr. Waters's speculative statement that G.B. could have suffered an "anamnestic response" to the hepatitis B vaccine, a point which Dr. Waters

[13] Dr. Waters classifies these three arms as the innate immune response, Type 1 hypersensitivity, and Type 2 hypersensitivity. (Ex. 12 at 10.)

relies upon as further increasing the likelihood of G.B. experiencing cytokine storm. (*Id*. at 5.)

Instead, Dr. McCusker asserts that there is no evidence in the record to support a conclusion that G.B. experienced the progressive signs of excessive cytokine activation. (Ex. A at 7.) While petitioner reported that G.B. displayed increased fussiness and decreased feeding in the period following vaccination, Dr. McCusker indicates that normal clinical patterns suggest that if he had experienced excessive cytokine activation, he "would have gotten very ill, developed very high fever and would have exhibited symptoms, such as, respiratory distress, unrelenting irritability and rash in the time period immediately prior to his death." (*Id*.)

Dr. McCusker also addresses Dr. Waters' conclusion that G.B. may have suffered Type I and Type II hypersensitivity reactions. Dr. McCusker defined Type I hypersensitivity as an allergic reaction, including anaphylaxis, that occurs within minutes or up to a few hours after exposure to a provoking agent, usually reaching peak severity within 5-30 minutes. (Ex. A at 7.) Signs and symptoms of such a reaction are found in the skin (hives and swelling), the gastrointestinal tract (*e.g.*, vomiting and diarrhea), the respiratory tract (*e.g.*, throat swelling, difficulty breathing, wheezing), and the cardiovascular system (low blood pressure). (*Id*.) Children who experience Type I hypersensitivity reactions display significant skin manifestations and persistent abdominal symptoms of pain and vomiting. (*Id*. at 8.) Dr. McCusker notes that G.B. displayed "no clinical features . . . consistent with an allergic reaction that would lead to the conclusion that his death was a result of or a component of an anaphylactic event." (*Id*.) Further, Dr. McCusker reports that there were no findings from G.B.'s autopsy that would lead to a conclusive diagnosis of anaphylaxis. (*Id*.)

As for Type II hypersensitivity, Dr. McCusker explains that such reactions occur when IgG "auto-antibodies" are formed. (Ex. A at 8.) She notes that Dr. Waters fails to provide any mechanism by which a Type II hypersensitivity could have contributed to G.B.'s death, except to state that cytokines could be released in this reaction. (*Id*.) Dr. McCusker explains, however, that this reaction is not caused by cytokine release and occurs over the course of several days to weeks. (*Id*. at 7.) Thus, even if G.B. experienced a Type II hypersensitivity reaction, it could not have contributed to the cytokine storm that Dr. Waters posits as leading to G.B.'s death within 24 hours after receiving his vaccinations. (*Id*. at 8.) In conclusion, Dr. McCusker contends that there is no clinical evidence G.B. suffered a cytokine storm. (*Id*. at 9.) She further opines that even if there were evidence of a cytokine storm, the mechanisms (i.e., the hypersensitivity reactions) proposed by Dr. Waters are not consistent with the current scientific literature. (*Id*.)

Instead, Dr. McCusker concurs with Dr. Kohlmeier's determination that G.B.'s death resulted from "probable positional asphyxia." (Ex. A at 9.) Nevertheless, she also evaluated the evidence that could support SIDS as an alternative cause of G.B.'s death. Dr. McCusker notes that epidemiological studies have identified extrinsic risk factors for sudden infant death syndrome (SIDS), including prone or side sleeping, bed sharing,

over-bundling, soft bedding, face covered, and recent history of upper respiratory tract infection. (*Id*. at 8.) In normal infants, environmental conditions/stressors, which can lead to transient changes in O_2/CO_2 balance, activate the protective mechanisms in the brain through the 5HT system and correct the problem.[14] (*Id*.) However, "at risk" children fail to correct this imbalance and suffer cardiorespiratory arrest. (*Id*.)

In addition, Dr. McCusker notes that studies have demonstrated clear association between sleep position, sleep location, and parental, especially maternal, smoking as significant risk factors for the development of SIDS. (Ex. A at 8.) With regard to maternal smoking, prenatal exposure to tobacco has been identified as contributing to the intrinsic vulnerability of an infant through impairment of central chemosensitivity and several neurotransmitter systems. (*Id*. at 9.) Prenatal nicotine exposure can also alter breathing patterns and reduce the hypoxia/hypercarbia induced ventilatory chemoreflexes. (*Id*.) In the case of G.B., petitioner reported that she placed him next to her in bed after a nighttime awakening and discovered him "lifeless" several hours later. (Ex. 3 at 2.) He was also exposed to maternal tobacco smoke during pregnancy.[15] Furthermore, Dr. McCusker explains that the location of lividity as reported in the autopsy suggests that G.B. was at least semi-prone, possibly prone (i.e. on his stomach), at the time of death. (Ex. A at 8.)

With regard to an association between vaccination and SIDS, Dr. McCusker notes that studies to analyze this connection have found no differences in the frequency or patterns of SIDS compared with the expected frequency in the population. (Ex. A at 9.) Instead, Dr. McCusker explains that well designed studies have shown findings against a causal association for SIDS and vaccines, providing strong epidemiological evidence for temporal association only. (*Id*. citing Traversa, G. et al., *Sudden Unexpected Deaths and Vaccinations During the First Two Years of Life in Italy: a Case Study*, PLoS One 2011 6:e16363 (Ex. EE); Venneman, M. et al., *Sudden Infant Death Syndrome: No Increased Risk After Immunisation*, Vaccine 2007 25:336-40 (Ex. FF); Kuhnert, R. et al., *Reanalysis of Case-Controlled Studies Examining the Temporal Association Between Sudden Infant Death Syndrome and Vaccination*, Vaccine 2012 30:2349-56 (Ex. GG). Dr. McCusker concludes by stating she "find[s] no evidence that the vaccination[s] on March 12, 2014 contributed to [G.B.'s] death. (*Id*.)

ii. Sara Vargas, M.D.

Respondent also provided an expert opinion from Dr. Sara Vargas, a pathologist. (Ex. C.) Dr. Vargas serves as a pathologist at three Boston area hospitals: Children's Hospital, Brigham and Women's Hospital, and the Dana Farber Cancer Institute. (Ex. D at 2). She is also an associate professor at Harvard University. (*Id*.) Dr. Vargas received her medical degree from the University of Vermont, completed a pathology

[14] The 5HT system senses changes in O_2 and CO_2 and is involved in regulating arousal from sleep, body temperature, auto-resuscitation, and the laryngeal chemoreflex. (Ex. A at 8.)

[15] Petitioner's antepartum records reflect that she was a smoker during her pregnancy with G.B. (Ex. 7 at 12-13.)

residency at Brigham and Women's Hospital, and trained as a fellow in pediatric pathology at Children's Hospital, Boston. (*Id*.) She is also a diplomate of the National Board of Medical Examiners and the American Board of Pathology (Anatomic, Clinical, and Pediatric Pathology). (*Id*. at 13.)

In evaluating G.B.'s case, Dr. Vargas initially noted that "[t]here are gaps in available information for assessing the main differential diagnosis," including the lack of findings from a scene investigation, witness interviews or other detailed police investigation, information about the position of G.B.'s body when it was found, information about petitioner's medications or any other ingestions proximate to G.B.'s death, and information about the conduct of individuals at the scene. (Ex. C at 6-7.) However, Dr. Vargas notes in her supplemental report, that she was subsequently was provided with autopsy and scene photos. (Ex. OO at 2.) She describes these photographs as showing "loose bedding composed of two quilted adult-sized bedcovers and at least four pillows." (*Id*.)

Dr. Vargas states that there are a number of factors identifiable in the available case material to support Dr. Kohlmeier's conclusion that G.B.'s cause of death as probable asphyxia due to co-sleeping. (Ex. C at 7.) Similar to Dr. McCusker, Dr. Vargas notes that factors potentially contributing to asphyxiation of G.B. include sleeping in an adult bed, sleeping with an adult, and prone sleep positioning. (*Id*. at 7.) Dr. Vargas explains that postmortem lividity, which occurs as a result of blood pooling after death, can also assist in determining body positioning at the time of death. (*Id*. at 6.) Scene photographs show G.B.'s body, in what appears to be an ambulance, with postmortem lividity of the left face, back, and arms. (Ex. OO at 2.)

Further, as discussed above, Dr. Kohlmeier's autopsy report reflects lividity on the anterior and posterior aspects of G.B.'s body, consistent with the photographs from autopsy reviewed by Dr. Vargas. (Ex. 4 at 1-2; Ex OO at 2.) Dr. Vargas explains that an infant's body is routinely placed face-up for CPR and morgue refrigeration, which can contribute to lividity on the posterior surfaces of the body. (Ex. C at 7.) In the case of G.B., as noted above, CPR was performed for 20-25 minutes and he was subsequently transported to the Oklahoma City Office of the Chief Medical Examiner, where an autopsy was performed the next day. (Ex. 4 at 1; Ex. 10 at 2.) While a more detailed scene investigation would be necessary to reach a definitive conclusion, Dr. Vargas reports that "it is most likely that the anterior lividity observed in G.B.'s body stemmed from prone positioning from the time of death until he was moved for CPR." (Ex. C at 7.) Dr. Vargas also notes that pleural petechial hemorrhage, as was observed in G.B., is commonly seen at autopsy in deaths from asphyxia, which further supports Dr. Kohlmeier's findings regarding G.B.'s cause of death. (*Id*.)

Similar to Dr. McCusker, Dr. Vargas notes that SIDS may be considered in the differential diagnosis of G.B.'s death. (Ex. C at 8, 11.) However, SIDS is a diagnosis of exclusion, and can only be made after asphyxia and other causes of death are ruled out. (*Id*. at 8.) Nevertheless, Dr. Vargas notes that G.B. did fit the appropriate age peak for SIDS of 1-6 months and his death apparently occurred during a period of sleep, in

the setting of co-sleeping with an adult in an adult bed, and likely in the prone position. (*Id*.) As described by Dr. McCusker, male gender and maternal smoking are risk factors for SIDS, and pleural petechiae (as was found in G.B.) can be found in deaths due to either SIDS or asphyxia. (*Id*.) In fact, Dr. Vargas states that deaths from asphyxia, especially while occurring during a sleep period, can mimic SIDS, and if evidence supporting asphyxia had not been recognized by Dr. Kohlmeier, then "SIDS would be a strong diagnostic consideration in this case." (*Id*.) Dr. Vargas also concurs with Dr. McCusker's conclusions regarding the involvement of vaccinations in this case by stating that "[v]accinations are not known to cause or contribute to asphyxia . . . or SIDS, and there is no evidence to suggest that they caused or contributed to G.B.'s death." (*Id*.) For reasons discussed in greater detail below, Dr. Vargas disagrees with Dr. Miller's interpretation of congestion and hemorrhage found during G.B.'s autopsy as suggesting a pathological bleeding disorder. (Ex. OO, pp. 4-5.)

Dr. Vargas also responds to the conclusions reached by Dr. Waters. (Ex. C at 8.) She agrees with Dr. Waters's conclusion that the autopsy findings do not "definitely" show that G.B. died of asphyxia and that there are other possibilities for a cause of death, including SIDS.[16] (*Id*. at 9, 11.) However, in contrast to Dr. Waters's statement that "co-sleeping is not a cause of death," Dr. Vargas indicates that infant asphyxia is a well-known complication of bed-sharing with adults, and bed-sharing is a well-known risk factor for SIDS. (*Id*. at 9.) Dr. Vargas asserts that "[a]lthough co-sleeping of course does not always lead to death, events that occur in the course of co-sleeping are well accepted to cause death" and "[i]t is nothing short of preposterous to state that [it] cannot cause death or that [it] can only cause death if the adult is impaired by alcohol or drugs," as claimed by Dr. Waters. (*Id*.) Dr. Vargas indicates that it is clear from Dr. Kohlmeier's report that she believed that an accident from co-sleeping caused an asphyxia death in G.B., and "for Dr. Waters to imply that such a case is not even possible seems disingenuous." (*Id*.) Finally, as for Dr. Waters's conclusion that G.B. suffered a lethal vaccine-mediated cytokine storm, Dr. Vargas states that such an allegation is unsupported and that the vaccines received by G.B. have not been shown to cause death due to cytokine storm. (*Id*. at 10-11.)

V. Discussion

In this case, G.B.'s official cause of death as determined by the Office of the Chief Medical Examiner of Oklahoma City is accidental death by probable asphyxiation due to co-sleeping. Petitioner seeks to displace that finding in favor of an immunological, cytokine-driven, explanation for G.B.'s death. Assessing petitioner's claim involves three overarching questions.

[16] Dr. Vargas also suggests that there is some autopsy evidence suggesting that G.B. may have suffered from congenital pancreatic islet cell hyperplasia, causing hyperinsulinemic hypoglycemia, which could have played a role in his death. (Ex. C at 7-8.) However, she acknowledges that without detailed scene (of death) information, it is impossible to surmise whether asphyxia or hyperinsulinemic hypoglycemia was the more likely cause. (*Id*. at 10.)

First, petitioner questions the medical examiner's decision to list asphyxiation as a certain, accidental cause of death in what might otherwise be classified as a case of Sudden Infant Death Syndrome ("SIDS"), i.e. an unexplained death. Deeming this a case of SIDS is prerequisite to petitioner's claim as it would facilitate her experts' exploration of alternative causes of death whereas accidental asphyxiation would be a mutually exclusive explanation of G.B.'s death. A petitioner must prove by a preponderance of the evidence the factual circumstances surrounding her claim. 42 U.S.C. § 300aa–13(a)(1)(A). Accordingly, petitioner's disagreement with G.B.'s recorded cause of death poses a threshold question. For the reasons discussed below, petitioner is not persuasive in contending that G.B.'s official cause of death is incorrect.

Second, operating on the premise that G.B.'s death is otherwise unexplained, petitioner advances the theory that G.B.'s vaccinations triggered a cytokine-mediated event, causing endothelial damage that led to hemorrhaging and congestion in multiple organs, and ultimately leading to his death. (ECF No. 51.) Petitioner's experts opine that what G.B. experienced was "an increased capillary permeability syndrome" (Ex. 12, p. 9 (Dr. Waters)) or an "acute visceral microvascular bleeding disorder" similar to a "primary or secondary 'capillary leak syndrome.'" (Ex. 22, p. 5 (Dr. Miller)). Both experts opine that this condition would have arisen as a consequence of an excessive cytokine response. (Ex. 12, p. 9; Ex. 22, p. 5.) Even setting aside the question of asphyxiation, application of the *Althen* test to this theory demonstrates that petitioner has not met her burden of proof in this case.

Third, and finally, because SIDS, though not fully understood, is believed to be multifactorial, if petitioner were correct that G.B.'s death was better explained as SIDS rather than as asphyxiation, this would raise a question of whether the leading model of SIDS (the Kinney or Triple Risk Model) offered any basis for including G.B.'s vaccinations among the multiple factors leading to his death. Confusingly, while Dr. Miller opines on petitioner's behalf that G.B. did not likely experience SIDS (Ex. 22, p. 6) he also at turns characterizes this as an instance of SIDS (*Id*. at 7) and concludes his initial report by directly paralleling his causal theory in this case to the causal theory he has presented in prior SIDS cases. (*Id*. at 8). For her part, Dr. Waters also suggested that a subset of SIDS cases may actually represent deaths due to immunization. (Ex. 12, p. 7.) These questions have received substantial attention in prior Program cases and Drs. Miller and Waters are not persuasive on these points.

a. Asphyxia is the Most Likely Cause of Death

At first blush, there is clearly no dispute that ultimately the injury at issue in this case is G.B.'s tragic death. Importantly, however, there is significant disagreement regarding the correct characterization of the manner and cause of G.B.'s death. As noted above, Dr. Kohlmeier, the medical examiner, concluded that the manner of G.B.'s death was accidental and the cause of death "probable asphyxia due to co-sleeping." (Ex. 4, p. 1.) Petitioner's experts disagree. Respondent argues, however, that "[w]hile the autopsy report alone does not *per se* bind the Special Master to adopt its conclusions (*see* 42 U.S.C. § 300aa-13(b)(1)), it is powerful and persuasive evidence in

this case, particularly since the medical examiner's findings were not rebutted by a second review of G.B.'s pathology slides three months after his death." (ECF No. 56, pp. 16-17.) Respondent's experts support the medical examiner's conclusion. [17]

Medical records generally constitute trustworthy evidence. *Cucuras v. Sec'y Health & Human Servs.*, 993 F.2d 1525, 1528 (Fed. Cir. 1993). Moreover, although rebuttable, the "medical records and medical opinion testimony" of treating physicians can be "quite probative," because "treating physicians are likely to be in the best position to determine whether 'a logical sequence of cause and effect show[s] that the vaccination was the reason for the injury.'" *Capizzano v. Sec'y of Health & Human Servs.*, 440 F.3d 1317,1326 (Fed. Cir. 2006) (quoting *Althen*, 418 F.3d at 1280); *accord Andreu v. Sec'y of Health & Human Servs.*, 569 F.3d 1367, 1376 (Fed. Cir. 2009). This principle has also been applied in the context of SIDS and asphyxia because, although not strictly speaking "treating" physicians, the opinions of coroners and medical examiners are based on their direct autopsy examinations and role in investigating the cause of death. *Pelton v. Sec'y of Health & Human Servs.*, No. 14-674V, 2017 WL 1101767, at *13 (Fed. Cl. Spec. Mstr. Feb. 27, 2017). As Drs. Waters and Miller alluded in their first reports, Dr. Kohlmeier's conclusion draws on two sources of information, the results of the autopsy itself and the scene information. (Ex. 12, p. 6; Ex. 22, p. 4.) Dr. Kohlmeier is the only physician to have examined G.B.'s body post-mortem. Drs. Rostad, Waters, Miller, and Vargas, relied on Dr. Kohlmeier's report and on the microscopic slides created during her examination. (Ex. 5, p. 1; Ex. 12, p. 3; Ex. 22, pp. 3-7; Ex. C, pp. 1-2.) Dr. Vargas further suggests that as the investigating medical examiner Dr. Kohlmeier likely had access to additional scene information unavailable to the experts in this case. (Ex. C, p. 6; Ex. OO, p. 1.) And, indeed, Dr. Kohlmeier is the only opining physician to have had access to the investigating officers at the scene. Accordingly, Dr. Kohlmier's conclusion should ordinarily be entitled to significant weight.

Petitioner's disagreement with Dr. Kohlmeier's conclusion stems in significant part from a differing perspective with regard to the relationship between SIDS, co-sleeping, and asphyxia, a question that is unsettled among pathologists. Sudden Infant Death Syndrome is not a diagnosis *per se*. Rather, it is a term applied to instances of infant death that remain unexplained. (E.g. Ex. 32, p. 1.) Accordingly, a determination that asphyxia has occurred constitutes an explanation of death that supplants the SIDS label. Dr. Waters explains that over time increased awareness of asphyxia as a cause of death has explained a significant portion of the decrease in reported incidence of

[17] The burden does not shift to respondent to demonstrate a factor unrelated to vaccination as the cause of G.B.'s death unless petitioner initially meets her burden of proof under the *Althen* test. § 300aa-13(a)(1)(B); *Walther v. Sec'y of Health & Human Servs.*, 485 F.3d 1146, 1150 (Fed. Cir. 2007). Importantly, however, respondent may also present evidence casting doubt on petitioner's case-in-chief, though petitioner does not bear the burden of eliminating alternative causes if she can otherwise meet her burden of proof under *Althen*. *de Bazan v. Sec'y of Health & Human Servs.*, 539 F.3d 1347, 1352-53 (Fed. Cir. 2008); *Walther*, 485 F.3d at 1150. When faced with disagreement among qualified experts regarding the identification and nature of a disputed injury, the Federal Circuit has concluded that it is "appropriate for the special master to first determine what injury, if any, [is] supported by the evidence presented in the record before applying the *Althen* test to determine causation." *Lombardi v. Sec'y of Health & Human Servs.*, 656 F.3d 1343, 1351-53 (Fed. Cir. 2011).

SIDS. (Ex. 12, p. 6.) However, in Dr. Waters's view, because asphyxia is difficult to diagnose pathologically, it is likely that it has been over-diagnosed. (*Id*.) Dr. Waters believes that in SIDS-type cases, the cause of death should remain undetermined rather than being identified as asphyxia. (*Id*.)

Dr. Miller further explains that current forensic pathology practice in this country is "discordant" regarding how to view the relationship between co-sleeping, asphyxia, and SIDS. (Ex. 22, p. 6.) According to Dr. Miller, co-sleeping may be considered a risk factor for SIDS, but the SIDS classification should not be set aside in favor of asphyxia as the cause of death based on sleeping conditions alone. (*Id*.) Rather, he would require direct evidence of entrapment (such as direct lying-over of the adult on the baby) to conclude there was an accidental asphyxia death. (*Id*.) Like Dr. Miller, Dr. Waters stresses that "if any specific lethal events occur, they should be included in the cause of death." (Ex. 23, p. 3.)

Dr. Miller acknowledges, however, that "many medical examiners refuse to make a diagnosis of SIDS in the setting of co-sleeping or even other presumed unsafe sleeping conditions." (Ex. 22, p.6.) Moreover, it appears that Dr. Miller is overly stringent in his suggestion of what would constitute evidence of asphyxiation. Describing the Triple Risk Mode of SIDS, he suggests that:

> SIDS research back to the work of Kinney and others has regarded sleeping conditions in carbon dioxide ("re-breathing") as a risk factor for SIDS, not as an alternative diagnosis which excludes SIDS. Co-sleeping, unless there is demonstration of actual entrapment of the baby's head (in the corner of a sofa, or under an adult's body), is in this line of analysis therefore not regarded as evidence of asphyxiation separate from SIDS.

(*Id*.)

For this proposition he cites Blair, et al, *Major epidemiological changes in sudden infant death syndrome: a 20-year population-based study in the UK*, 367 Lancet 314 (2006) (Ex. 32). Review of that paper indicates, however, that for purposes of the study cases were excluded from the definition of SIDS in instances of suspected overlay or asphyxia "when the evidence on balance of probability (including histopathological findings, review of history, and death-scene investigation), showed such a cause." (Blair, et al., *supra*, at Ex. 32, p. 2.) As described further below, this is consistent with Dr. Kohlmeier's report and nothing in this paper indicates that demonstrated entrapment of the head is specifically required to evidence asphyxiation separate from SIDS as Dr. Miller suggests.

Additionally, although the difference between documenting a death as SIDS or asphyxia may touch on important research or public policy considerations, there is an extent to which, in the specific context of this case, Drs. Miller and Waters are engaging in semantics by raising the distinction between co-sleeping as a risk factor for SIDS on the one hand and asphyxia due to co-sleeping being a reported cause of death on the other. Dr. Waters in particular stresses that "co-sleeping is not a cause of death." (Ex.

12, p. 10.) This framing of the issue has been previously criticized. *Pelton*, 2017 WL 1101767, at *11 (explaining that "Dr. Waters suggests that because most co-sleeping infants do not die, co-sleeping can be considered only a risk factor and not a cause of death. That co-sleeping does not lead to death in many or even most instances does not preclude it from being identified as a cause of death when, as here, evidence supports that conclusion.") And, indeed, in this case Dr. Vargas responds sharply to this point, indicating that "[a]lthough co-sleeping of course does not always lead to death, events that occur in the course of co-sleeping are well accepted to cause death. It is nothing short of preposterous to state that they cannot cause death . . ." [18] (Ex. C, p. 8.)

Setting aside Dr. Waters's specific statements, Dr. Miller's report further illustrates the semantic issue. Dr. Miller is critical of respondent's expert, Dr. Vargas, because she "goes through all the risk factors for SIDS imposed on this baby by the terminal sleeping condition, but does not explicitly deal with these as risk factors for SIDS, instead she agrees with the ME that they suggest probable asphyxiation." (Ex. 22, p. 6.) However, Dr. Miller also explains that under the Triple Risk Model "the prevailing hypothesis in the SIDS research community [is] that an infant without any medullary defects will arouse when inhaled CO2 levels cause hypercapnia,[19] *even if the hypercapnia is a consequence of the unsafe sleeping condition*." (*Id*. (emphasis added).) What Dr. Miller reveals is that while the SIDS model proposes that there may be additional underlying vulnerabilities that help explain why reduced oxygen and re-inhaled carbon dioxide ultimately becomes fatal in these cases, even under the SIDS model the risk posed by co-sleeping still ultimately relates to a direct relationship between the unsafe sleeping conditions and a deficiency of breathable air, i.e., suffocation or asphyxia. Regardless of whether the death is labeled on a death certificate or autopsy report as SIDS or asphyxiation, the actual hazard initially posed by unsafe sleeping conditions is the same. Thus, standing alone, the distinction being drawn by petitioner's experts between asphyxiation and SIDS provides very little basis for calling Kohlmeier's report into question regarding her review of the circumstances and scene.

This point is further underscored by the literature filed by petitioner. According to Li, et al, "[p]lacing infants to sleep on surfaces shared with another person or persons exposes them to potentially fatal hazards. These hazards include overlay by cosleeper; entrapment/wedging between the bedding and cosleeper or between mattress and wall,

[18] It is also interesting to note that there is a degree of internal tension in Dr. Waters's opinion. Dr. Waters opines in effect that SIDS is now underreported due to the increase in reports of asphyxiation but also suggests that SIDS may be overreported vis-à-vis what she considers deaths due to vaccine toxicity. (Ex. 12, pp. 6-7.) When it comes to an association between co-sleeping and death, Dr. Waters seems to contend that the statistical association alone is not enough to implicate co-sleeping as a cause of death via accidental asphyxiation. However, in suggesting that a subset of SIDS is actually caused by vaccination, Dr. Waters seeks to rely entirely on the same type of associational evidence only far weaker (in fact, relying more broadly on the overall infant mortality rate).

[19] Hypercapnia refers to an excess of carbon dioxide in the blood. (*Dorland's Illustrated Medical Dictionary*, p. 876 (33rd ed. 2020).)

head entrapment in bed railings, and suffocation on soft bedding or waterbeds." (Li, et al., *Observations on Increased Accidental Asphyxia Deaths in Infancy While Cosleeping in the State of Maryland*, 30 Am J Forensic Med Pathol 318-321 (2009) (Ex. 13, p. 4). This was based on a review of 102 infant deaths in Maryland. (*Id.* at 1.) Following a retrospective study of nine years of infant death data from Kentucky, Knight, et al, similarly observe with regard to co-sleeping as a risk factor for unexpected infant death that:

> the actual hazard may also be related to confounding factors which create an unsafe cosleeping environment, such as cosleeping on couches and other unsafe surfaces (including beds too small for the number of individuals sleeping); soft bedding, pillows, and comforters; parental intoxication or exhaustion when cosleeping; cosleeping with adults who smoke; and cosleeping with noncaregivers, or nonelective cosleeping with a disinterested caregiver due to socioeconomic factors.

(Knight, et al., *Cosleeping and Sudden Unexpected Infant Deaths in Kentucky, a 10-Year Retrospective Case Review*, 26 Am J Forensic Med Pathol 28-32 (2005) (Ex. 14, p. 5.).

Whereas Dr. Miller acknowledges co-sleeping to be a risk factor for SIDS generally (Ex. 22, p. 6), Dr. Waters further opines that co-sleeping is not even a risk factor absent drug or alcohol impairment. (Ex. 12, p. 10). Dr. Waters cites three articles as support for her contention that co-sleeping is a SIDS risk factor only in the presence of drug or alcohol impairment - the above-discussed Li, et al., and Knight, et al., as well as a third article by Blair, et al. (Blair, et al., *Bed-Sharing in the Absence of Hazardous Circumstances: Is There a Risk of Sudden Infant Death Syndrome? An Analysis from Two Case-Control Studies Conducted in the UK*, 9(9) PLoS ONE e107799 (2014) (Ex. 15).) Only Blair, et al, directly addresses this point. Blair, et al, sought to further investigate specific co-sleeping environments. Examining 405 infant deaths from two prior studies, the Blair authors found that when adjusting for other SIDS risk factors, the overall risk of SIDS for co-sleeping infants was almost four-fold. (*Id*. at 3.) However, once the data was further broken down by sleeping environment and age, only those cases associated with the hazards of drug or alcohol use, smoking, or sleeping in a sofa or chair, remained statistically significant. (*Id*. at 4.) Notably, however, this study confirms that among variables there was a strong interaction with age that demonstrated a higher risk from co-sleeping for infants less than three months of age. (*Id*. at 4.) G.B. was about two months old at the time of his death. (Ex. 2, p. 7.)

The Blair authors also explain that "[w]e have largely established potential associations rather than causal factors and can only interpret the findings in terms of the factors we have recorded." (Blair, et al., *supra*, at Ex. 15, p. 5.) They note that:

> [t]he combined dataset is relatively large for case-control studies and is population-based with very few missed deaths during the study period but is only large enough to look at a dichotomy of interactions amongst the

> multiple categories of co-sleeping death and even then the numbers for some categories may be small as reflected by the large confidence intervals of risk estimates.

(*Id*. at 5.)

In any event, the authors concluded that their results should further suggest that accidental asphyxiation explains the relationship between SIDS and co-sleeping. (*Id*.) Blair, et al, provides a more nuanced perspective regarding the risks of infant co-sleeping. However, it is not in itself evidence rebutting Dr. Kohlmeier's conclusion. Like Li, et al, and Knight et al., it does support an overall association between co-sleeping and infant death. Moreover, it underscores the overarching understanding that co-sleeping is associated with SIDS precisely because of the danger of accidental asphyxiation.

Petitioner's reliance on SIDS to discount Dr. Kohlmeier's conclusion as to asphyxia is all the more tenuous given that Dr. Miller does not actually opine that G.B. experienced SIDS. Although he agrees that findings of pulmonary edema and pleural petechiae are consistent with SIDS, his observation that there was congestion and hemorrhage in other organs coupled with his inability to detect any medullary defect (a hallmark of the Triple Risk Model of SIDS), has led him to opine that "this case does not fit the most common SIDS scenarios, vaccinations or no vaccinations (or at least as far as the autopsy evidence permits, it does not fit)." (Ex. 22, p. 6.) According to Dr. Miller, under the Triple Risk Model, the presence of a medullary defect explains why an infant may not arouse in response to hypercapnia. (*Id*. at 5.) This renders Dr. Miller's opinion inconsistent and somewhat incoherent in that it is not clear why Dr. Miller favors the SIDS/CO_2 rebreathing explanation over what he characterizes as "simple" asphyxiation given the lack of any medullary defect consistent with that explanation.

Instead, the thrust of the opinions offered by Dr. Waters and Dr. Miller seems to be merely to challenge the very idea that G.B.'s death is explainable, such that their exploration of additional hypotheses would be reasonable. In that regard they appear to be suggesting that the risk that co-sleeping will lead to asphyxiation is not enough, standing alone, to conclude that asphyxia due to co-sleeping was the actual cause of G.B.'s death. Petitioner's experts are correct that in general a statistical association is not equivalent to proof of causation. However, they are not persuasive in suggesting that this negates Dr. Kohlmeier's determination of the cause of death in this case. Dr. Kohlmeier's conclusion cannot be reduced simply to reliance on a statistical observation regarding the risks of co-sleeping. Nor are petitioner's experts otherwise persuasive in suggesting any factor specific to this case that would suggest this individual case represents an over-use of asphyxiation as the cause of death.[20]

[20] Dr. Miller did note that G.B.'s brain weight was considered heavy for his age, but without evidence of cerebral edema or brain herniations. According to Dr. Miller, this is a "common if poorly understood" finding in SIDS cases that differentiates this case from "simple" asphyxiation. (Ex. 22, p. 6.) Dr. Miller is unpersuasive on this point. First, Dr. Miller does not explain how or why this finding would differentiate this case from one of asphyxia. This lack of explanation is especially notable given that Dr. Miller acknowledges the finding to be one of poorly understood significance even in the SIDS context. Second,

Dr. Kohlmeier's reported pathology findings are consistent with SIDS, which is to say they are also consistent with asphyxia and do not point to any other obvious cause of death. Dr. Kohlmeier observed no trauma based on either internal or external examination and also concluded that G.B. was a normally-developed and well-nourished infant. (Ex. 4, p.1- 2.) Post-mortem toxicology was negative. (*Id*. at 1.) There was no evidence of infection or tumor relative to either the nervous or respiratory systems. (*Id*. at 2-3.) With regard to positive findings, Dr. Kohlmeier observed "a small amount of petechial hemorrhages" in the lungs and also congestion of the lungs on microscopic examination. (*Id*. at 3-4.) Both of petitioner's experts, Dr. Waters and Dr. Miller, agree that these petechial hemorrhages are consistent with SIDS without respect to the specific cause of death. (Ex. 12, p. 5; Ex. 22, p. 4.) Respondent's pathology expert, Dr. Vargas, similarly agrees, but further stresses that the finding also supports asphyxia specifically given the context of prone sleeping. (Ex. C, p. 6.) With regard to the microscopic evidence of congestion, Dr. Miller and Dr. Vargas both agree that this is also consistent with SIDS, though Dr. Miller characterizes the degree of congestion in this case as atypically severe.[21] (Ex. 22, p. 4; Ex. C, p. 5.) Petitioner also had an independent autopsy conducted by Dr. Rostad. (Ex. 5.) Dr. Rostad additionally agreed that the autopsy findings were non-specific but consistent with asphyxia. (*Id*.)

In the setting of pathology consistent with SIDS, the more specific conclusion that asphyxia was the cause of death primarily derives from evidence relating to co-sleeping. There is no dispute in this case that G.B.'s death occurred in the context of co-sleeping. Petitioner averred that prior to his death, she had placed G.B. beside her in her bed after a diaper change at around 4:30-5:00 a.m. (Ex. 3, p. 2.) Scene photographs also show that G.B. had been sleeping on a bed with soft, loose bedding, which has been identified in the relevant literature as hazardous.[22] (*E.g.* Shapiro-Mendoza, et al., *Trends in Infant Bedding Use: National Infant Sleep Position Study*, 1993-2010, 135 Pediatrics 1 (2015) (Ex. AA); *see also* Li, et al., *supra*, at Ex. 13, p. 4; Knight, et al., *supra*, at Ex. 14, p. 5.) Additionally, the observations on autopsy are significant for

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Dr. Miller ultimately opines that he does not believe this child's autopsy findings "fit the most common SIDS scenarios." (*Id*.) Dr. Miller cannot credibly contend that a specific finding should be viewed as confounding the medical examiner's assessment of asphyxia on the basis that it is consistent with SIDS while simultaneously opining that SIDS is not the correct explanation for the child's death. Dr. Miller offers no explanation as to why G.B.'s brain weight supported his alternative assessment of a visceral microvascular bleeding disorder. In any event, Dr. Vargas refutes that G.B.'s brain weight was unusually heavy. (Ex. OO, p. 4.)

[21] Dr. Waters acknowledges the finding, but did not specifically opine regarding its significance. (Ex. 12, p. 5.)

[22] Dr. Kohlmeier's autopsy report does not specifically describe what she reviewed with regard to the scene, but does confirm she was aware of the co-sleeping arrangement and was in contact with the Mike Barker, the reporting officer. (*Compare* Ex. 4, p. 6 and Ex. 9, p. 5.) Petitioner subsequently filed a CD containing "autopsy and scene photos." (ECF No. 20.) Accompanying petitioner's notice were 14 photographs taken in the course of the autopsy and 20 scene photographs taken by the first responders, including photographs of G.B. on scene as well as several photos clearly documenting the sleeping environment.

revealing that G.B. was likely prone at the time of death. Specifically, Dr. Miller and Dr. Vargas both explain that the autopsy photographs confirmed the presence of both anterior and posterior lividity, the anterior lividity indicates G.B.'s body was face down initially while the posterior lividity is due to the post-mortem storage of his body on its back.[23] (Ex. 22, p. 3.) Dr. Waters further observes that G.B.'s face had purple lividity on the left and blanching on the right. (Ex. 12, p. 5.) She opines that this "suggest[s] the right side was pressed against something and the left side was somewhat down." (*Id*.) Notwithstanding the above-discussed disagreements regarding the relationship between SIDS, asphyxia, and co-sleeping, these factors, which suggest G.B. was co-sleeping on soft, loose bedding and prone, face down, and with his face pressed against something, are consistent with the medical examiner's conclusion that the circumstances of G.B.'s death, when combined with his autopsy results otherwise negative for any explanation apart from SIDS, were consistent with an accidental death due to asphyxia.

While Dr. Waters and Dr. Miller both express concern about possible overuse of asphyxia as a cause of death, Dr. Miller in particular acknowledges that this issue is unsettled among forensic pathologists and that Dr. Kohlmeier would not be outside the mainstream of the field if she refused to label the death as unexplained SIDS in the context of an unsafe sleeping environment. (Ex. 22, p. 6.) And, in any event, even if petitioner's experts were persuasive in suggesting that it would be better policy for G.B.'s cause of death to be recorded as SIDS rather than asphyxia, Dr. Miller acknowledges that the SIDS model could still point to the unsafe sleeping conditions as the initiating cause of the fatal hypercapnia when such conditions are present. (*Id*.) Accordingly, petitioner's experts are not persuasive in suggesting that Dr. Kohlmeier's report should be viewed as incorrect based on either the broader conventions of the relevant medical community or the prevailing understanding of SIDS.[24]

b. Petitioner's Theory of a Cytokine-Mediated Adverse Event Fails the *Althen* Test

Instead of either asphyxiation or SIDS, petitioner argues that G.B.'s vaccinations triggered a cytokine-mediated event, causing endothelial damage that led to hemorrhaging and congestion in multiple organs and ultimately his death. (ECF No. 51.) Petitioner's experts opine that what G.B. experienced was "an increased capillary permeability syndrome" (Ex. 12, p. 9 (Dr. Waters)) or an "acute visceral microvascular

[23] Dr. Waters suggests that the combination of posterior and anterior lividity does not indicate which side G.B. was on at the time of death. (Ex. 12, p. 5.) However, this does not account for Dr. Miller's and Dr. Vargas's explanation that G.B. would have been kept on his back post-mortem. Dr. Waters has previously been found unpersuasive on this point in a prior case. *See Pelton*, 2017 WL 1101767, at *13.

[24] Of note, Dr. Miller also highlights certain pathology findings that he views as confounding as to either asphyxia or SIDS, but which he contends support petitioner's theory of causation. Specifically, he opined that congestion and hemorrhaging in multiple organs supports a microvascular bleeding disorder These findings are separately discussed in section V(b)(ii)(2), below. For the same reasons discussed therein, they are not persuasive in calling Dr. Kohlmeier's conclusion into question.

bleeding disorder" similar to a "primary or secondary 'capillary leak syndrome'" (Ex. 22, p. 5 (Dr. Miller)). Both experts opine that this condition would have arisen as a consequence of an excessive cytokine response. (Ex. 12, p. 9; Ex. 22, p. 5.) For the reasons discussed below, these opinions are inadequate to meet petitioner's burden of proof under the applicable three-part *Althen* test.

i. *Althen* Prong One

Petitioner's burden under the first *Althen* prong is to provide, by preponderant evidence, "a medical theory causally connecting the vaccination and the injury." *Althen*, 418 F.3d at 1278. Such a theory must only be "legally probable, not medically or scientifically certain." *Knudsen v. Sec'y of Health & Human Servs.*, 35 F.3d 543, 549 (Fed. Cr. 1994). Moreover, scientific evidence offered to establish *Althen* prong one is viewed "not through the lens of the laboratorian, but instead from the vantage point of the Vaccine Act's preponderant evidence standard." *Andreu*, 569 F.3d at 1380. However, to satisfy this prong, petitioner's theory must be based on a "sound and reliable medical or scientific explanation." *Knudsen*, 35 F.3d at 548; *Boatmon*, 941 F.3d at 1359. With this standard in mind, I conclude that upon review of Dr. Waters's and Dr. Miller's reports, the literature they have cited, and Dr. Vargas's and Dr. McCusker's competing opinions, petitioner has not met her burden of demonstrating a medical theory causally linking G.B.'s death and his vaccinations.

Both Dr. Waters and Dr. Miller opine that elevated cytokines can cause endothelial cell dysfunction leading to some form of capillary leak or bleeding disorder. (Ex. 12, p. 9; Ex. 22, p. 5.) As the first to opine, Dr. Waters initially relied on the concept of a cytokine storm and indicated that such a state can produce capillary permeability and plasma leakage as seen in dengue fever. (Ex. 12, p. 9.) Dr. Miller indicates, however, that this is not a "prototypical" cytokine storm and instead indicates that "the occurrence of severe congestion with hemorrhages in many organs in the absence of any prior evidence for a coagulopathy implicates a diffuse systemic cytokine-mediated problem of small vessel (capillary) integrity." (Ex. 22, p. 8.) He instead analogizes G.B.'s condition to "systemic capillary leak syndrome" ("SCLS"). (*Id.*) In that regard, petitioner relies on six publications discussing SCLS. (Ex. 22 (citing Robin, *supra*, at Ex. 34; Lofdahl, et al., *Systemic capillary leak syndrome with monoclonal IgG and complement alterations. A case report on an episodic syndrome*, 206 Acta Med Scand. 405-12 (1979) (Ex. 35); Kawabe, et al., *Capillary Leak Syndrome*, 41 Int Med 211-15 (2002) (Ex. 36); Hsu, et al, *Idiopathic capillary leak syndrome in children*, 135 Pediatrics e730-e735 (2015) (Ex. 37); Kulihova, et al., Fatal primary capillary leak syndrome in a late preterm newborn, 3 Indian J. Pediatr. 1197-1199 (2016) (Ex. 38); Siddall and Radhakrishnan, Capillary leak syndrome: etiologies, pathophysiology, and management, 92 Kidney International 37-46 (2017) (Ex. 40)).)

SCLS is a rare disorder in which a constellation of symptoms appear that are related to increased permeability of capillaries to proteins. (Siddall and Radhakrishan, *supra*, at Ex. 40, p. 1.) This results in edema and hypotension, and in some cases can

lead to hypovolemic[25] shock and multiple organ failure. (*Id*.) There are several conditions known to result in SCLS, including sepsis, viral hemorrhagic fevers, and some autoimmune diseases. (*Id*.) It can also be drug-induced or idiopathic. (*Id*.) As of 2015 there had only been between 200-300 reported cases of SCLS since it was first described in 1960. (Hsu, et al., *supra*, at Ex. 37, p. 1.) Petitioner filed a case report of a newborn infant dying from suspected capillary leak syndrome. (Kulihova, et al., *supra*, at Ex. 38.) However, that child died 27 days after birth with low blood pressure and respiratory distress being observed within the first day of life. (*Id*. at 1-2.) No cause for the infant's condition was identified and there is no confirmation that any vaccines were administered or suspected as a possible cause of the condition. (*Id*.)

Some literature filed by petitioner does hypothesize that the capillary permeability to protein underlying SCLS may be related to hypercytokinemia (Siddall and Radhakrisnan, *supra*, at Ex. 40, p. 4); however, other literature cited by petitioner cautions that the pathophysiology is unclear and cytokines are not necessarily the leading consideration (Hsu, et al., *supra*, at Ex. 37, p. 5 (primarily discussing monoclonal gammopathy and noting that "other soluble factors such as cytokines could also have a role.") Dr. McCusker stresses that to the extent elevated cytokines have been observed in SCLS patients, it remains unclear whether they are pathogenic or merely markers or manifestations of SCLS. (Ex. NN, p. 3.) Notably, SCLS is more common in healthy young and middle-aged adults (Kawabe, et al., *supra*, at Ex. 36, p. 2) and among pediatric cases "the absolute levels of all cytokines were much lower in the children tested than those seen in adults" (Hsu, et al., *supra*, at Ex. 37, pp. 5-6). Importantly, while viral infection has been associated with SCLS (*e.g*. Kawabe, et al., *supra*, at Ex. 36, p. 2[26]), none of the literature in this case posits or even suggests any suspicion that vaccination could be a cause or trigger of SCLS. Dr. McCusker explains that investigation of the cytokines elevated in SCLS suggests that a TH1 profile is consistent with preceding viral infection. (Ex. NN, p. 3 (citing Druey and Parikh, *Idiopathic Systemic Capillary Leak Syndrome (Clarkson disease)*, 1430(3) J Allergy Clin Immunol. 663-670 (2017) (Ex. NN, Tab 1)).) Conversely, Dr. McCusker cites a study by Hingorani, et al, that demonstrated that vaccination may blunt the type of vasodilation that precedes capillary leak, suggesting that the types of cytokines produced by vaccination are not implicated in SCLS. (Ex. NN, p. 3 (citing Hingorani, et al., *Acute Systemic Inflammation Impairs Endothelium-Dependent Dilation in Humans*, 102 Circulation 994-999 (2000) (Ex. K)).)

Cytokines are small protein chemicals secreted by cells for the purpose of intercellular signaling and communication. (Ex. 18 at 2; Ex. A at 4.) Their functions include the regulation of angiogenesis and immune and inflammatory responses. (*Id*.) Further, cytokines occur naturally, are present in humans in both healthy and diseased states, and are responsible for everyday homeostasis. (Ex. C at 9; Ex. NN at 5.) Not all

[25] Hypovolemia is "abnormally decreased volume of circulating blood in the body." (*Dorland's*, 33rd ed., p. 896.)

[26] Noting that "[a]lthough the precise mechanism of SCLS has not been elucidated, Amoura et al suggested that viral infection might trigger the attacks because man of the patients had experienced preceding episodes of flu-like illness." (Ex. 36, p. 2 (citation omitted).)

cytokines are proinflammatory. (Ex. A, p. 3.) Thus, the simple presence of cytokines does not imply that cytokines have caused injury. (Ex. A; Ex. C.) There is no disagreement among the experts in this case that vaccination induces the release of cytokines to at least some degree. (Ex. A, p. 3.) However, to the extent Dr. Waters and Dr. Miller opine broadly that elevated cytokines could lead to a catastrophic injury, the evidence of record does not support their conclusion that the ordinary cytokine response to vaccination could in itself be implicated in either a cytokine storm or SCLS-like endothelial injury. Petitioner has not filed any literature demonstrating vaccination to be a cause or trigger of either SCLS or cytokine storm. Instead, Drs. Miller and Waters seek to marry via their *ipse dixit* literature showing elevated proinflammatory post-vaccination cytokines on the one hand with literature showing SCLS and cytokine storm as being injurious cytokine-mediated conditions on the other. However, the literature filed in this case demonstrates only that cytokine levels observed post-vaccination are dramatically lower than the levels of cytokines measured in those experiencing injurious systemic cytokine reactions. There is nothing on this record demonstrating that the cytokines elicited by vaccination lead to uncontrolled systemic reactions.

For example, Hingorani, et al, injected 12 healthy subjects with a capsular polysaccharide typhoid vaccine and compared cytokine levels based on blood samples taken immediately before and up to eight hours after vaccination. (Hingorani, et al, *supra*, at Ex. K, p. 2.) IL-1β was 4.7 pg/mL at baseline and rose to 5.0 pg/mL, a 0.3 pg/mL difference the authors characterized as "no change." (*Id*. at 3 (Table).) IL-6 was 2.1 pg/mL at baseline and increased to 3.4 pg/mL. IL-1Ra was 188 pg/mL at baseline and rose to 593.6 pg/mL. (*Id.* at 3 (Table).) The authors also observed that there had been no change in concentration of TNF-α, but did not show the data. (*Id*. at 3.) In contrast, Dr. McCusker cited a case study of six previously healthy control subjects from a clinical trial who experienced a cytokine storm within 90 minutes of receiving a single intravenous dose of a monoclonal antibody treatment, which is designed to provoke the immune system. (Suntharalingam, et al., *Cytokine Storm in a Phase 1 Trial of the Anti-CD28 Monoclonal Antibody TGN1412*, 355 N Engl J Med 10 (2006) (Ex. M).) According to Dr. McCusker this is [t]he best documented series of clinical events that occur when cytokines are inappropriately activated . . ." (Ex. A, p. 6.) In these cases IL-1β rose to about 5,000 pg/mL, IL-6 rose to between 3,000 to 4,000 pg/mL, and TNF-α rose to between 4,000 and 5,000 pg/mL. (Suntharalingam, et al., *supra*, at Ex M, p. 8 (Figure 3C).) Thus, for example, the increased levels of IL-1β and IL-6 during a cytokine storm were 1,000-times the level observed post-vaccination in the Hingorani, et al, study.

Additionally, Drs. McCusker and Miller provide competing interpretations of the significance of a study by Kashiwagi, et al., which is a paper filed by both parties. (Yasuyo Kashiwagi et al., *Production of Inflammatory Cytokines in Response to Diphtheria-Pertussis-Tetanus (DPT), Haemophilus Influenzae Type B (Hib), and 7-Valent Pneumococcal (PCV7) Vaccines*, 10(3) Human Vaccines & Immunotherapeutics 677 (2014) (Ex. 31; Ex. L).) Kashiwagi, et al, examined post-vaccination cytokine levels in two ways. First, the study authors drew 29 blood samples from healthy children from which peripheral blood mononuclear cells ("PBMCs") were obtained. (Kashiwagi, et al.,

supra, at Ex. 31, p. 3.) These PBMC cultures were then stimulated with various combinations of diphtheria tetanus and acellular pertussis vaccine, Haemophilus influenza b vaccine, and 7-valent pneumococcal vaccine. (*Id*.) Second, the study authors obtained serum samples 24 hours post-vaccination from 61 vaccine recipients who experienced a febrile response and 18 who did not. (*Id*.) These groups were compared to each other and to a group of 18 samples taken from patients in the influenza H1N1 outbreak and nine patients experiencing acute pneumonia. (*Id*.) According to Dr. McCusker, Kashiwagi, et al., is significant for showing (1) that overall levels of cytokines remained low post-vaccination and (2) that post-vaccination fever developed independently of cytokine levels. (Ex. A, p. 6.) Dr. McCusker suggests this constitutes a lack of evidence that vaccination can increase cytokine levels to an injurious degree as seen in a cytokine storm. (*Id*.) Dr. Miller counters that the significance of the Kashiwagi, et al., study is that it showed post-vaccination cytokine levels to be comparable to the levels seen among influenza infection patients. (Ex. 22, p. 7.) He further contends that influenza infections have in turn been documented to induce a cytokine storm, intimating that vaccinations must therefore also be capable of inducing a cytokine storm. (*Id*.)

Although Kashiwagi, et al, did produce elevated levels of cytokines by artificially stimulating PBMCs, they acknowledged that "an experiment in which PBMCs were stimulated with vaccine antigen did not necessarily reflect the in vivo responses following vaccination." (Kashiwagi, et al, *supra*, at Ex. 31, p. 7.) In contrast, comparing the febrile vaccine recipients, non-febrile vaccine recipients, and unvaccinated controls, Kashiwagi, et al., observed:

> No detectible IL-1β was observed in sera in both febrile and non-febrile groups and no significant difference was observed in cytokine levels of IL-6 and TNF-α between the two groups . . . The mean serum levels of inflammatory cytokines IL-1β, IL-6, and TNF-α were 0.68, 29.44, and 13.43 pg/ml in vaccine recipients with febrile reactions after the simultaneous injection of three (DPT/Hib/PCV) or four vaccines (DPT/Hib/PCV+ other vaccine), and similar levels of inflammatory cytokines were produced in vaccine recipients with febrile reactions after immunization of one or two inactivated bacterial vaccines, also similar to those in non-febrile group. . . Higher levels of IL-6, Il-10, Il-12, G-CSF, IFN-γ, and TNF-α were detected in both febrile and non-febrile groups after vaccination in comparison with those in normal subjects.

(*Id*. at p. 4.)

These in vivo results are far closer (by orders of magnitude) to the post-vaccination measurements taken by Hingorani, et al., than they are to the type of cytokine increases observed among the six confirmed cytokine storm cases discussed above. Accordingly, Dr. McCusker's interpretation of Kashiwagi appears sound. Dr. Miller is also correct that the study showed post-vaccine cytokine levels comparable to certain influenza infections; however, the authors note that cytokine levels among

vacinees were comparable only to "mild-moderate outpatients" infected with influenza. (Ex. 22, p. 7; Kashiwagi, et al., *supra*, at Ex. 31, p. 7.) Moreover, Kashiwagi, et al, cautioned that even among their cohort of hospitalized infection patients, "extremely serious patients were not included in the hospitalized patient group." (*Id*.) And, importantly, nothing in this paper suggests that any of the study subjects experienced cytokine-mediated adverse events following either vaccination or infection. Thus, although Dr. Miller suggests that *some* influenza infections can induce a cytokine storm, he has not substantiated that those infections are at all comparable to the "mild-moderate" infections studied by Kashiwagi, et al., or that those other instances had a cytokine profile comparable to those demonstrated by Kashiwagi, et al.

In fact, Dr. McCusker cites literature demonstrating that the levels of inflammatory cytokines among pandemic strain influenza infections do correlate to the severity of illness. (Zhou, et al., *Avian Influenza A (H7N9) viruses isolated from patients with mild and fatal infection differ in pathogenicity and induction of cytokines*, 111 Microbial pathogenesis 402-09 (2017) (Ex. NN, Tab 8); Beigel, et al., *Avian influenza A (H5N1) infection in humans*, 353 N Engl J Med 1374-85 (2005) (Ex. NN, Tab 9); Liu, et al., *The cytokine storm of severe influenza and development of immunomodulary therapy*, 13 Cellular & molecular immunology 3-10 (2016) (Ex. NN, Tab 10); Hagau, et al., *Clinical aspects and cytokine response in severe H1N1 influenza A virus infection*, 14 Critical care R203 (2010) (Ex. NN, Tab 11).) In contrast, Dr. McCusker cites an additional study, Barria, et al., which found "no predictable patterns could be detected in the measured cytokines" following vaccination with a live attenuated influenza vaccine ("LAIV"). (Barria, et al., *Localized Mucosal Response to Intranasal Live Attenuated Influenza Vaccine in Adults*, 207 JID 115 (2013) (Ex. J, p. 6).) The authors indicated that "in contrast to virus infection, LAIV does not appear to trigger a change in serum cytokine profiles."[27] (*Id*.) While the Barria, et al., study does not negate the Kashiwagi, et al., findings, it underscores the difficulty in attempting to extrapolate the effects of vaccination as compared to infection, especially when juxtaposed with the above-discussed literature relating to pandemic infections as cited by Dr. McCusker. On the whole, Dr. Miller is not persuasive in suggesting that Kashiwagi, et al., itself provides evidence that any vaccinations – alone or in combination – elevate cytokines to a degree or in a manner that could be consistent with petitioner's theory.[28]

Dr. Miller's opinion is essentially limited to citing Kashiwagi, et al., to note the parallel between vaccinations eliciting cytokines to any degree and SCLS being a potentially cytokine-mediated condition. He leaves entirely unaddressed the question of

[27] Dr. Miller is critical of Dr. McCusker's reliance on this study because it measured cytokine levels three-days post vaccination whereas he stresses that G.B. died within 24 hours of vaccination and further stresses that cytokine levels peak between 24 and 48 hours after inoculation. (Ex. 22, pp. 7-8.) However, the study authors indicate that they were comparing their findings to the rises in cytokines occurring during viral infection which they indicated occurs over 48-72 hours. (Barria, et al., *supra*, at Ex. J, p. 6.)

[28] Of note, Dr. Miller does appear to imply that his theory may be further supported by the idea that the Triple Risk Model of SIDS accounts for otherwise trivial infections becoming fatal. (Ex. 22, p. 8.) This is unpersuasive for the reasons discussed in Section V(c), below.

how an ordinarily mild cytokine response to vaccination becomes an uncontrolled and catastrophically injurious systemic condition. (Ex. 22, pp. 7-8.) In fact, he explicitly indicates that "in this instance the vaccinations triggered cytokine responses (as usual) *which for reasons unknown* set off a cascade of events with endothelial damage in multiple organs leading to hemorrhages and congestion found at autopsy . . ." (*Id*. at 8 (emphasis added).) Given that the above-discussed literature demonstrates only a mild cytokine response to vaccination, and given that none of the SCLS literature cited by Dr. Miller so much as suspects that vaccines trigger SCLS, Dr. Miller's reliance on this parallel without more would be entirely speculative even in the absence of Dr. McCusker's refutation.

Dr. Waters does seek to provide some further explanation by invoking G.B.'s multiple vaccinations,[29] possible anamnestic response from his prior Hepatitis B exposure, and the role of Type I and Type II hypersensitivity responses. (Ex. 12, p. 8.) However, these factors are not well explained. Moreover, Dr. McCusker notes that G.B.'s presentation was not consistent with any Type I hypersensitivity reaction (i.e. anaphylaxis) and a Type II hypersensitivity reaction is not consistent with petitioner's cytokine-mediated theory. (Ex. A, pp. 6-7.) Dr. Miller also acknowledges that G.B. had no clinical signs or autopsy evidence of anaphylaxis. (Ex. 22, p. 7.) After challenge by Dr. McCusker, Dr. Waters seems to indicate that the import of her initial discussion was merely that "vaccines stimulate cytokines." (Ex. 23, p. 2.)

Dr. Waters also cites an article providing an overview of cytokine storms, including their relationship to capillary permeability (most notably in relation to dengue fever). (Tisoncik, et al., *Into the Eye of the Cytokine Storm*, 76(1) Microbiology and Molecular Biology Reviews 16-32 (2012) (Ex. 18).) This article discusses some of the susceptibilities that could help explain how a cascading cytokine response leads to a cytokine storm; however, the article focuses on cytokine storms as following viral respiratory infections and does not include any discussion of vaccinations. (*Id*.) Dr. McCusker explains that the immune response to infection is not comparable to the immune response to vaccination. In natural infection there are pattern recognition receptors that upregulate gene expression of the innate immune system and

[29] Kashiwagi, et al., stimulated PBMCs both with individual vaccinations and different combinations of up to three vaccinations and examined 17 different cytokine profiles. Comparing single vaccination to concurrent vaccination, they found no significant difference among ten of the profiles (IL-2, IL-4, IL-5, IL-7, IL-10, IL-12, IL-13, IL-17, GM-CSF, and IFN-γ. (Kashiwagi, et al., *supra*, at Ex. 31, p. 5.) There were differences among IL-1β, IL-6, G-CSF, and TFN-α; however, the results do not reflect any correlation between the number of antigens or vaccinations and the degree of inflammation. (*Id*. at p. 4 (Figure 1).) For example, mean levels of IL-1β do appear to have increased as the number of vaccines increased. However, mean levels of IL-6 were higher for Hib alone than they were for any combination of multiple vaccines. Combining three vaccines (DPT/Hib/PCV) resulted in lower mean IL-6 than any of the combinations of two vaccines. Mean concentration of TNF-α was also lower when PMBCs were stimulated with DPT, Hib, and PCV than when stimulated with only Hib and PCV. (*Id*.) The authors also noted that "[c]ytokine production was examined in PBMCs culture stimulated with IPV, influenza, and MR vaccines and very low levels of inflammatory cytokines were produced (data not shown). Therefore, additional simultaneous immunization [is] supposed to have little influence on cytokine induction in sera." (*Id*. at p. 7.)

inflammatory response correlates to live virus shedding, which is not a factor in vaccination. (Ex. A, p. 4.) Given the differing areas of specialty, Dr. McCusker is better qualified than either Dr. Waters or Dr. Miller to speak both to the immunology underlying cytokine storms and SCLS as well as the immune response to vaccination.

In sum, there is inadequate evidence of record to demonstrate that petitioner's experts have presented a sound and reliable medical theory of causation implicating any vaccine(s) in causing cytokine-mediated endothelial damage resulting in multiple organ hemorrhaging. As explanation for how this may occur, petitioner advances two conditions as proxy: a cytokine storm and/or SCLS. However, although active and severe infections have been associated with both SCLS and cytokine storms, petitioner has not demonstrated that vaccines have previously been implicated, or even could be implicated, in the process of either SCLS or cytokine storms. Vaccines do elicit an inflammatory cytokine response, but the above-discussed literature shows the ordinary vaccine response to be mild and orders of magnitude less than what is seen in a cytokine storm. Petitioners have not otherwise demonstrated that the mild response to vaccination could lead to uncontrolled systemic cytokine response in the same manner as an active infection.

ii. *Althen* Prong Two

The second *Althen* prong requires proof of a logical sequence of cause and effect connecting vaccination and injury, usually supported by facts derived from a petitioner's medical records. *Althen*, 418 F.3d at 1278; *Andreu*, 569 F.3d at 1375–77; *Capizzano*, 440 F.3d at 1326; *Grant*, 956 F.2d at 1148. However, medical records and/or statements of a treating physicians do not *per se* bind the special master to adopt the conclusions of such an individual, even if they must be considered and carefully evaluated. *See* Section 13(b)(1) (providing that "[a]ny such diagnosis, conclusion, judgment, test result, report, or summary shall not be binding on the special master or court"); *Snyder v. Sec'y of Health & Human Servs.*, 88 Fed. Cl. 706, 746 n.67 (2009) ("there is nothing ... that mandates that the testimony of a treating physician is sacrosanct—that it must be accepted in its entirety and cannot be rebutted").

Here, as discussed above, the evidence preponderates in favor of asphyxiation as the cause of G.B.'s death as found by the investigating medical examiner, a cause of death not consistent with petitioner's theory. Additionally, petitioner has not demonstrated by preponderant evidence that G.B.'s vaccinations *can cause* either a cytokine storm or an SCLS-like hemorrhagic injury. These findings are fundamentally at odds with any showing that G.B.'s vaccinations *did cause* his death as required under *Althen* prong two. However, there are also additional significant reasons why petitioner would be unable to demonstrate a logical sequence of cause and effect showing G.B.'s vaccinations to be the cause of his death even in the absence of these incompatible findings.

1. G.B.'s post vaccination presentation does not indicate excessive cytokine reaction.

Initially, Dr. Waters opined that G.B. had in fact suffered a "cytokine storm." (Ex. 12, pp. 8-10.) However, Dr. McCusker explains that a "cytokine storm" is a rare condition that has been described in specific disease states. (Ex. A, p. 5.) Inflammation associated with a cytokine storm begins at a local site and spreads throughout the body via systemic circulation. (Ex. 18 at 4.) The hallmarks of acute inflammation include rubor (redness), tumor (swelling or edema), calor (heat), dolor (pain), and "functio laesa" (loss of function). (*Id*.) According to Dr. McCusker, a cytokine storm constitutes a severe illness including not merely unrelenting irritability, but also rash, high fever, and respiratory stress. (Ex. A, p. 6.) Those suffering a cytokine storm are "profoundly ill." (*Id*.) According to Dr. McCusker, this does not describe G.B.'s presentation prior to his death. (*Id*.) Dr. Miller likewise agrees on petitioner's behalf that a cytokine storm is not a useful concept in this case. He notes that "[t]his is not a prototypical case of 'cytokine storm,' a term used to describe fatal or near-fatal events in the setting of severe infection with, usually, septicemia, which is clearly not the case here." (Ex. 22, p. 8.) Thus, in her supplemental report Dr. Waters ultimately suggests she was relying on an increase in cytokines regardless of "whether or not there was clinical or pathological evidence of an actual 'cytokine storm.'" (Ex. 23, p. 4.) She does not, however, explain on what basis G.B.'s presentation would otherwise be consistent with a systemic cytokine response.

Dr. Miller also initially relied on petitioner's report that post-vaccination G.B. was not aroused once he fell asleep, demonstrating "something more than normal sleep," as well as a persistent refusal to feed. (Ex. 22, p. 7 (citing Ex. 3).) Dr. Miller stressed this as "continuously abnormal behavior of the child from the time of vaccination until death." (*Id*.) He acknowledged, however, that fussiness following a needle stick is common for an infant and that he cannot say that what petitioner described constituted a coma. (*Id*. at 6-7.) After being asked by the previously presiding special master to explain the importance of petitioner's description of G.B.'s post-vaccination behavior, Dr. Miller indicates that the behavior is "of some importance," but nonetheless explains that:

> the interpretation of the autopsy findings and my conclusions as to their most likely cause, and thus the cause of death, would not change if I was told that the symptoms and signs reported by the mother were not, in fact, present. Since the bulk of my conclusions are from the autopsy and not from the history, very little in my report would change other than to take away the recitation of symptoms and signs which the mother alleged the child exhibited.

(Ex. 24.)

For purposes of this decision, I accept as accurate petitioner's recollection of G.B.'s behavior on March 12, and 13, 2014. (Ex. 3.) However, even accepting his reported behavior as abnormal for him, the behaviors described are non-specific and

Dr. Miller acknowledges the difficulty in drawing medical conclusions from these reports in the absence of a medical exam. (Ex. 22, pp. 6-7; *see also* Ex. C, p. 6.) Ultimately, petitioner describes G.B. as unusually sleepy, unusually fussy ("beyond fussy" and "miserable"), crying, and uninterested in feeding. (Ex. 3, p. 2.) These behaviors were concerning enough that petitioner contemplated contacting G.B.'s pediatrician, but not so concerning that petitioner sought emergency care. (*Id.*) Again, Dr. McCusker stresses the absence of any indication of fever or rash that would indicate cytokine activation. (Ex. A, pp. 5-6.) She also stresses that excessive cytokine activation would have resulted in progressive illness, including high fever and respiratory distress, which is not the presentation described by petitioner. (*Id*.) Dr. Miller also acknowledges that G.B. had no clinical signs or autopsy evidence of anaphylaxis. (Ex. 22, p. 7.) Moreover, a case series of six pediatric cases of SCLS filed by petitioner showed that all six children experienced flulike prodrome that consisted not merely of lethargy, but also variously included nasal inflammation (coryzal symptoms), leg or abdominal pain, fever, vomiting, periorbital swelling and/or headache, swelling, and in some instances diarrhea or cough, later leading in most instances to edema and/or shock. (Hsu, et al., *supra*, at Ex. 37, p. 4 (Table 1).) G.B.'s presentation does not suggest any flulike prodrome comparable to what was documented among the pediatric SCLS subjects. Accordingly, there is not preponderant evidence that G.B.'s clinical presentation prior to his death was consistent with petitioner's theory of causation.

2. G.B.'s autopsy results do not indicate a SCLS-like condition.

Dr. Miller has expressed general agreement with the observations of Dr. Rostad, who conducted an independent review of petitioner's autopsy for petitioner, and stresses the severe congestion and hemorrhaging in multiple organs beyond the lungs first noted by Dr. Rostad. (Ex. 22, p. 4.) Specifically, Dr. Miller notes congestion and petechial hemorrhaging in the kidneys, adrenal glands, and medulla. (*Id*.) He describes these as "not typical" for SIDS. (*Id*.) He also notes "frank" hemorrhage in the lungs, more than could be attributed to post-mortem spillage, as well as severe congestion at the periphery of the hepatic lobules of the liver. (*Id*. at 4-5.) According to Dr. Miller, these are the findings that support the presence of a microvascular bleeding disorder. (*Id*. at 5.) There are two significant reasons why Dr. Miller's opinion is unpersuasive.

First, Dr. Vargas explains that G.B.'s post-mortem findings are not as atypical as Dr. Miller suggests. The hemorrhaging evidenced in G.B.'s lungs is consistent with trauma from cardiopulmonary resuscitation. (Ex. OO, p. 4.) The blood vessels in the lungs are especially fragile following hypoxia and death. (*Id*.) In contrast, SCLS is characterized by proteinaceous fluid and alveolar damage. (*Id*.) Dr. Vargas further indicates that there is a lack of evidence of inflammation or hemosiderosis[30] to suggest that any of the bleeding happened prior to resuscitation. (*Id*.) Dr. Vargas additionally cites literature demonstrating that 40% of SIDS cases have adrenal congestion and 3% have adrenal hemorrhage. (Ex. OO, p. 5 (citing Valdes-Dapena, et al., *Histopathology Atlas for the Sudden Infant Death Syndrome, Findings derived from the National*

[30] Hemosiderosis is "a focal or general increase in tissue iron stores without associated tissue damage." (*Dorland's*, 33rd ed., p. 833.)

Institute of Child Health and Human Development Cooperative Epidemiological Study of Sudden Infant Death Syndrome (SIDS) Risk Factors, 1993 (Ex. QQ).) Kidney congestion is seen in 26% of SIDS cases. (Vadles-Dapena, et al., *supra*, at Ex. QQ, p. 9.) Twenty-eight percent of SIDS cases have congestion evidenced in the brain while 17% show perivascular hemorrhage in the brain and 16% have petechiae in the brain. (*Id.*) Citing a textbook example of a normal post-mortem liver (*Id.* at p. 3), Dr. Vargas disagrees that G.B.'s liver demonstrated congestion. (Ex. OO, p. 5.) For these reasons, Dr. Vargas indicates that there is no reason for Dr. Miller to even posit a pathologic bleeding disorder as the cause of death. (*Id.*) Indeed, despite noting similar observations as those raised by Dr. Miller, Dr. Rostad concurred with Dr. Kohlmeier in that he found the findings overall to be not specific and potentially explainable by asphyxia. (Ex. 5, p. 1.)

Second, respondent's experts are persuasive in indicating that G.B.'s autopsy on the whole is not consistent with an SCLS-like presentation. As the literature filed by petitioner demonstrates, the "leakage" typically associated with SCLS is of plasma. (*E.g.*, Kawabe, et al., *supra*, at Ex. 36, p. 2 (noting SCLS to be characterized by "recurrent episodes of generalized edema and hypovolemic shock."); Kulihova et al., *supra*, at Ex. 38, p. 1 (noting SCLS to be "characterized by episodes of vascular collapse and plasma extravasation, which may lead to multiple organ failure.").) Accordingly, Drs. Vargas and McCusker both explain that SCLS first and foremost presents with edema rather than hemorrhage as suggested by Dr. Miller; however, no edema was present upon G.B.'s autopsy. (Ex. NN, pp. 3-4; Ex. OO, p. 4.) Dr. Miller indicates that "[s]ome cases of this syndrome have associated hemorrhages, not just leakage of plasma," but this explanation acknowledges hemorrhages to be a less common manifestation of SCLS while also providing no support for the idea that SCLS could be evidenced by hemorrhaging in the absence of edema or other indicators of SCLS. (Ex. 22, p. 8.) Dr. McCusker in particular stresses that "the pathology of 'visceral petechial hemorrhagic process' described by Petitioners' [*sic*] Expert has **never** been described as an isolated effect of cytokine activation." (Ex. NN, p. 4 (emphasis original).)

iii. *Althen* Prong Three

The third *Althen* prong requires establishing a "proximate temporal relationship" between the vaccination and the injury alleged. *Althen*, 418 F.3d at 1278. That term has been equated to the phrase "medically-acceptable temporal relationship." *Id.* A petitioner must offer "preponderant proof that the onset of symptoms occurred within a timeframe which, given the medical understanding of the disorder's etiology, it is medically acceptable to infer causation." *de Bazan v. Sec'y of Health & Human Servs.*, 539 F.3d 1347, 1352 (Fed. Cir. 2008). The explanation for what is a medically acceptable timeframe must also coincide with the theory of how the relevant vaccine can cause an injury (*Althen* prong one's requirement). *Id.*; *Shapiro v. Sec'y of Health & Human Servs.*, 101 Fed. Cl. 532, 542 (2011), *recons. den'd after remand*, 105 Fed. Cl. 353 (2012), *aff'd mem.*, 503 Fed. Appx. 952 (Fed. Cir. 2013); *Koehn v. Sec'y of Health & Human Servs.*, No. 11–355V, 2013 WL 3214877 at *26 (Fed. Cl. Spec. Mstr. May 30,

2013), *mot. for review den'd* (Fed. Cl. Dec. 3, 2013), *aff'd*, 773 F.3d 1239 (Fed. Cir. 2014).

Petitioner argues that cytokine levels peak between 24-48 hours after vaccination. (Ex. 22 at 7-8.) She asserts that because G.B. died within 24 hours of vaccination, his adverse reaction and death fit within an appropriate timeframe for a diffuse systemic cytokine-mediated event leading to endothelial dysfunction and resulting in hemorrhage and congestion of the organs and subsequent death. (ECF No. 51, pp. 20-21.) Importantly, however, while Dr. McCusker filed literature suggesting that a cytokine storm can in general occur in as little as 90 minutes, it is less clear that the specific type of capillary leak that petitioner hypothesizes occurs so quickly. The timing of peak cytokine levels is not necessarily equivalent to the time over which capillary leak and hemorrhage manifest.

Among the six cytokine storm patients described in Suntharalingam, et al., most did not experience symptoms comparable to the capillary leak and hemorrhage hypothesized by petitioner. (*See* Ex. M, pp. 6-8.) Two patients did experience increased peripheral vascular permeability, but that presentation is described as occurring subsequent to 48 hours. (*Id*. at 8.) Moreover, Dr. Waters cites dengue fever as a relevant analogy given that hemorrhagic fever is known to be associated with SCLS. The literature she filed with respect to cytokine storms indicated that the increased capillary permeability seen in dengue fever typically occurs after between four to six days of illness. (Tisoncik, et al., *supra*, at Ex. 18, p. 11.) In the single case report of an infant death related to SCLS filed by petitioner, after onset of SCLS the infant experienced a fourteen-day period of no improvement before multiple organ dysfunction subsequently became fatal on the 27th day of life. (Kulihova, et al., *supra*, at Ex. 38, p. 2.) Although treatments were attempted during that period, massive capillary leak progressed and there was no recovery stage observed during the patient's life. (*Id*.) In Hsu, et al, four out of six pediatric subjects presented with shock and/or edema after experiencing at least 48 hours of prodromal symptoms. (*See* Ex. 37, pp. 2-3.) All of this raises a question as to whether the mere fact that cytokine response is generally known to occur rapidly is sufficient to explain a death by capillary leak and hemorrhage within 24 hours of an immune stimulus, especially in the absence of significant prodromal symptoms.

Both Dr. Miller and Dr. Waters are correct in noting that G.B.'s tragic death occurred within a relatively short time period after his vaccination. However, the significance of the temporal relationship must be tied to a reasonable theory of how the vaccines could have caused the death and then logically how they did cause the death. *See Grant*, 956 F.2d at 1144. A temporal relationship by itself is not sufficient to establish causation, even though it may reinforce a reasonable theory and logical explanation. *See Langland v. Sec'y of Health & Human Servs*., 109 Fed. Cl. 421 (2013). In this case, neither a persuasive and reliable theory nor a logical explanation of cause and effect were provided, leaving the potential temporal relationship standing alone. Moreover, even the significance of that purported temporal relationship remains unclear on this record. Accordingly, petitioner has failed to prove prong three of the *Althen* test.

c. Sudden Infant Death Syndrome Does Not Itself Otherwise Support Vaccine-Causation

Petitioner is not alleging that G.B. died of SIDS. (ECF No. 51, p. 11.) And, indeed, Dr. Miller opines on petitioner's behalf that, while the risk factors that are typical in SIDS cases would statistically make SIDS the most likely scenario in this case, the lack of histopathological abnormalities of G.B.'s medulla and the presence of the marked congestion and hemorrhage seen in multiple organs argue against this conclusion. (Ex. 22 at 5-6.) He therefore concludes that "this case does not fit the most common SIDS scenarios, vaccinations or no vaccinations (or at least as far as the autopsy evidence permits, it does not fit)." (*Id*. at 6.)

However, at the conclusion of his initial report, Dr. Miller suggests that his opinion is further supported by a parallel between his opinion in this case and his opinion in prior SIDS cases. (Ex. 22, p. 8.) Specifically, he states that:

> The occurrence of this syndrome, mediated by cytokines, following onset of an otherwise not life-threatening upper respiratory infection, suggests a parallel with the association of otherwise trivial upper respiratory infections with other cases of SIDS in which the pathogenesis is believed to involve peripherally generated cytokines interacting with developmentally defective medullary respiratory control systems . . .

(*Id*.)

The import of this statement appears to be that, notwithstanding that Dr. Miller does not opine that G.B. experienced SIDS, he nonetheless believes that the Kinney or Triple Risk Model of SIDS helps to explain why otherwise safe levels of cytokine activity could lead to death. Dr. Waters additionally indicates that in her view "[i]t is likely" that some cases now classified as SIDS are "caused by immunizations, which are given in quantity around the time these deaths tend to occur: 1-6 months of age." (Ex. 12 at 7.)

Petitioner's specific theory in this case of how vaccination may have led to G.B.'s death is addressed separately above. Here I note in the interest of completeness that, even if petitioner was correct that G.B.'s death was better classified as SIDS rather than asphyxiation, it would still not be the case that the multifactorial SIDS concept supports any role for G.B.'s vaccinations in causing his death.

There have been a significant number of prior cases in this Program that have addressed allegations that one or more childhood vaccines caused or contributed to a SIDS-labeled death. Generally, such cases have been dismissed by the presiding special masters for insufficient evidence that any vaccine played a causal role in the death.[31] In some instances, the parties have litigated whether SIDS presents an

[31] *See*, *e.g.*, *Olasvicky v. Sec'y of Health & Human Servs*., No. 17-1806V, 2019 WL 2881009 (Fed. Cl. Spec. Mstr. June 4, 2019); *Nunez v. Sec'y of Health & Human Servs*., No. 14-863V, 2019 WL 2462667

alternative cause of what petitioners otherwise alleged to have been a vaccine-caused death. *See, e.g.*, *Doe/11 v. Sec'y of Health & Human Servs.*, 601 F.3d 1349, 1351 (Fed. Cir. 2010) (holding that "the special master did not commit legal error in considering evidence of SIDS, an allegedly alternative cause. Nothing in the Vaccine Act prohibits the government from presenting evidence that the petitioner's injury was due to "factors unrelated" to the vaccine (here, SIDS)."). However, many of these prior cases have directly addressed at length allegations that one or more vaccines directly caused or contributed to a child's death within the framework of SIDS. In these prior decisions special masters generally found that attempts to establish vaccination as an exogenous stressor under the accepted Triple Risk (or Kinney) Model of SIDS were unpersuasive. *See, e.g.*, *Jewell,* 2016 WL 5404165 at *13; *Copenhaver,* 2016 WL 3456436 at *12-13; *Lord,* 2016 WL 806818 at *14; *Cozart,* 2015 WL 6746616 at *13. Additionally, the Federal Circuit has twice considered, and rejected, Dr. Miller's causal theory linking vaccinations to SIDS via the Triple Risk Model. *Boatmon*, 941 F.3d at 1351; *Nunez v. Sec'y of Health & Human Servs.,* 825 F. App'x 816 (Fed. Cir. 2020). I have also addressed the significance of these prior decisions and the question of whether vaccines contribute to the Triple Risk Model of SIDS as exogenous stressors in two prior cases. *Downing-Powers v. Sec'y of Health & Human Servs.,* No. 15-1043V, 2020 WL 4197303 (Fed. Cl. Spec. Mstr. June 2, 2020); *Brunson v. Secretary of Health & Human Servs*., No. 17-530V, 2020 WL 5755502 (Fed. Cl. Spec. Mstr. Sept. 3, 2020).

Several significant short-comings have prevented petitioners from relying on the Kinney or Triple Risk Model as providing a basis for supposing under *Althen* prong one that vaccination could play a role in SIDS-type deaths. The Federal Circuit explained in *Boatmon* that "outside of Vaccine Act litigation, vaccinations have not been identified as an exogenous stressor for SIDS." *Boatmon*, 941 F.3d at 1360. The Federal Circuit noted that petitioners' "extension of the Triple Risk Model to include vaccination-induced cytokine activity in the list of exogenous stressors" was based on "nothing more than the assertion of [petitioner's expert] Dr. Miller." *Id*. at 1361-62. As I explained in *Downing-Powers*, at least two serious obstacles remain in Dr. Miller's prior *ipse dixit* effort to

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(Fed. Cl. Spec. Mstr. Mar. 29, 2019), review denied 144 Fed. Cl. 540 (2019); *Frady v. Sec'y of Health & Human Servs*., No. 16-148V, 2017 WL 5379391 (Fed. Cl. Spec. Mstr. Sept. 20, 2017); *Pelton v. Sec'y of Health & Human Servs.*, No. 14-674V, 2017 WL 1101767 (Fed. Cl. Spec. Mstr. Feb. 27, 2017); *Jewell v. Sec'y of Health & Human Servs.*, No. 11-138V, 2016 WL 5404165 (Fed. Cl. Spec. Mstr. Aug. 29, 2016); *Copenhaver v. Sec'y of Health & Human Servs.*, No. 13-1002V, 2016 WL 3456436 (Fed. Cl. Spec. Mstr. May 31, 2016), *review denied*, 129 Fed. Cl. 176 (2016); *Lord v. Sec'y of Health & Human Servs.*, No. 12-255V, 2016 WL 806818 (Fed. Cl. Spec. Mstr. Feb. 9, 2016); *Cozart v. Sec'y of Health & Human Servs.*, No. 00-590V, 2015 WL 6746616 (Fed. Cl. Spec. Mstr. Oct. 15, 2015), review denied, 126 Fed. Cl. 488 (2016); *Waterman v. Sec'y of Health & Human Servs.*, No. 13-960V, 2015 WL 4481244 (Fed. Cl. Spec. Mstr. June 30, 2015), review denied 123 Fed. Cl. 564 (2015); *Sanchez v. Sec'y of Health & Human Servs.*, No. 11-651V, 2013 WL 4476750 (Fed. Cl. Spec. Mstr. Jul. 26, 2013); *Bigbee v. Sec'y of Health & Human Servs.*, No. 06-663V, 2012 WL 1237759 (Fed. Cl. Spec. Mstr. Mar. 22, 2012); *Nordwall v. Sec'y of Health & Human Servs.*, No. 05-123V, 2008 WL 857661 (Fed. Cl. Spec. Mstr. Feb. 19, 2008); *Doe/11 v. Sec'y of Health & Human Servs.*, 2008 WL 649065 (Fed. Cl. Spec. Mstr. Jan. 31, 2008); *Heller v. Sec'y of Health & Human Servs*., No. 96-797V, 1998 WL 408612 (Fed. Cl. Spec. Mstr. June 22, 1998); but see *Boatmon v. Sec'y of Health & Human Servs*., No. 13-611V, 2017 WL 3432329 (Fed. Cl. July 10, 2017*), review granted, decision rev'd*, 138 Fed. Cl. 566 (2018), *aff'd on other grounds*, 941 F.3d 1351 (Fed. Cir. 2019).

connect vaccination to that SIDS model. Studies seeking out a possible correlation between vaccinations and SIDS have not on the whole supported any association between the two and the evidence relied upon by Dr. Miller in linking peripheral cytokine response to vaccination to the serotoninergic network implicated by the Triple Risk Model is also very weak. 2020 WL 4197303 at *11-15. Thus, Dr. Miller's *ipse dixit* extension of the Triple Risk Model, which he himself previously characterized as merely plausible, has been considered unreliable.

Here, neither Dr. Waters nor Dr. Miller has provided information that would resolve these deficiencies. In suggesting that some SIDS cases may be vaccine-related, Dr. Waters cites a single study suggesting that infant mortality rates correlate with the number of vaccines recommended in developed countries. (Ex. 12, p. 7 citing Miller, Neil Z., and Gary S. Goldman, *Infant mortality rates regressed against number of vaccine doses routinely given: Is there a biochemical or synergistic toxicity?*, 30(9) Human and Experimental Toxicology 1420-28 (2011) (Ex. 16).) Importantly, however, this study examines only the overall infant mortality rate for each country against the number of vaccine doses included in the childhood immunization schedule of that country. (Miller and Goldman, *supra*, at Ex. 16, p. 1.) The study authors caution that a limitation of their study is that they did not adjust for national vaccine coverage rates and further acknowledge that the study is susceptible to ecological bias, meaning that "without additional data we do not know whether it is the vaccinated or unvaccinated infants who are dying in infancy at higher rates."[32] (*Id*. at 7-8.) Additionally, with respect to his separate cytokine theory discussed above, Dr. Miller's opinion continues to be premised on the same Kashiwagi article (*see* Kashiwagi, et al., *supra*, at Ex. 31), that I have previously discussed as being inadequate to demonstrate that a peripheral cytokine reaction to vaccination would affect the central nervous system in a manner consistent with the Triple Risk Model. *Downing-Powers*, 2020 WL 4197303, at *13; *Brunson*, 2020 WL 5755502, at *13. No other evidence of record in this case speaks to the issues explained by prior decisions with respect to a theory of causation based on the Triple Risk Model.[33]

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[32] Additionally, as in prior cases, Dr. McCusker offers competing studies that she indicates demonstrate that there is no relationship between vaccination and SIDS. (*See* Ex. A, p. 9 citing Traversa, et al., *supra*, at Ex. EE; Venneman, et al., *supra*, at Ex. FF; Kuhnert, et al., *supra*, at Ex. GG).)

[33] Special masters reasonably draw upon their experience in resolving Vaccine Act claims. *Doe v. Sec'y of Health & Human Servs.,* 76 Fed. Cl. 328, 338–39 (2007) ("[o]ne reason that proceedings are more expeditious in the hands of special masters is that the special masters have the expertise and experience to know the type of information that is most probative of a claim"). Nonetheless, special masters are not bound by the prior decisions of other special masters. *Hanlon v. Sec'y of Health & Human Servs.*, 40 Fed. Cl. 625, 630 (1998). In contrast, Federal Circuit rulings concerning legal issues are binding on special masters. *Guillory v. Sec'y of Health & Human Servs.*, 59 Fed. Cl. 121, 124 (2003), *aff'd* 104 F. Appx. 712 (Fed. Cir. 2004); *see also Spooner v. Sec'y of Health & Human Servs.*, No. 13-159V, 2014 WL 504728, at *7 n.12 (Fed. Cl. Spec. Mstr. Jan. 16, 2014). However, the Federal Circuit has also stressed that "[c]ausation in fact under the Vaccine Act is ... based on the circumstances of the particular case." *Boatmon*, 941 F.3d at 1358-59 (quoting *Knudsen*, 35 F.3d at 548). Accordingly, Federal Circuit precedents do not automatically control the outcome of subsequent cases even when they involve the same injury. *See, e.g.*, *Sanchez v. Sec'y of Health & Human Servs.*, 809 Fed. Appx. 843, 851-52 (Fed. Cir. 2020) (citing back to a prior Federal Circuit holding in *Paluck v. Secretary of Health & Human Services* involving the same injury and noting that "while there are substantial parallels between this case

Also significant is that a key reason that Dr. Miller does not opine that G.B. suffered SIDS was his observation that:

> Of particular note for a death in which at least some circumstances suggest SIDS, the medulla sections document a robust acruate nucleus on the ventral surface of each medullary phyramd (important because in some SIDS cases this nucleus is absent or hypolastic, and this is thought to play an important role in the pathophysiology of SIDS deaths in such cases).

(Ex. 22, p. 5.)

As has been explained in prior cases, the type of medullary defect described by Dr. Miller as important to the pathophysiology of SIDS (and absent in this case) is the basis for his previously presented hypothesis that post-vaccination cytokines could play a causal role in SIDS under the Triple Risk Model. *See, e.g. Boatmon*, 941 F.3d at 1356 (explaining that "[a]ccording to Dr. Miller's theory, '[w]hen the vaccines are administered in the presence of the defects in the medulla, during the critical developmental period, they are likely to have a similar effect as mild infection that may cause a failure of the medullary response system and ultimately a death.'") This also appears by extension to be his basis for supposing that an association between trivial infections and SIDS could be relevant to the different cytokine theory he presents in this case. However, even assuming the medullary defect was consistent with Dr. Miller's theory,[34] the Federal Circuit in *Boatmon* held that it was an abuse of discretion for the special master to rely for purposes of *Althen* prong two on the statistical probability of such a defect in the absence of any confirmatory evidence. 941 F.3d at 1362. Here, evidence of the defect is not merely lacking. Dr. Miller has confirmed this defect is actually absent. Accordingly, Dr. Miller has no basis for invoking a defective medullary respiratory control system in seeking to explain how G.B. could have been fatally susceptible to an otherwise "usual" post-vaccination cytokine response. (Ex. 22, p. 8.) Thus, even if I were to accept Dr. Miller's parallel as evidence supporting his theory under *Althen* prong one (which I do not), the absence of a medullary defect would then be fatal to petitioner's claim on *Althen* prong two. Accordingly, a finding that G.B. experienced SIDS rather than asphyxiation would not lend any further support to petitioner's claim.

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and *Paluck*, the differences between the two cases are such that the outcome of this case is not dictated by *Paluck*.").

[34] The Federal Circuit in *Nunez* held that it was "logical and reasonable" for the special master to conclude that the presence of a medullary defect is *contrary* to Dr. Miller's theory that cytokines can affect the medullary serotonin system. 825 Fed. Appx. at 820. This obviously raises a further question regarding the specifics of Dr. Miller's reliance on the Triple Risk Model; however, it is unnecessary to reach that question in this case.

d. Respondent's Contention of an Additional Factor Unrelated to Vaccination.

In the interest of completeness, I note that in addition to all of the above, respondent's pathology expert, Dr. Vargas, additionally questioned whether G.B.'s death might be explained by hyperinsulinemia hypoglycemia due to congenital pancreatic islet cell hyperplasia. (Ex. C, p. 6.) Petitioner's experts disagree. (Ex. 22, p. 4; Ex. 23, p. 3.) However, for all the reasons discussed above, the burden of proof did not shift to respondent to demonstrate any factor unrelated to vaccination. § 300aa-13(a)(1)(B). Accordingly, I do not reach the question of whether there is preponderant evidence that G.B. suffered fatal hypoglycemia as suggested by Dr. Vargas.

VI. Conclusion

G.B.'s death is tragic and a profound loss for his family. Petitioner has my deepest sympathy. However, upon my review of petitioner's claim, petitioner has not established by preponderant evidence that any of G.B.'s vaccinations caused his death. Accordingly, this petition is **DISMISSED**.[35]

IT IS SO ORDERED.

s/Daniel T. Horner
Daniel T. Horner
Special Master

[35] In the absence of a timely-filed motion for review of this Decision, the Clerk of the Court shall enter judgment accordingly.